13 October 2017
EMA/399493/2017 Revision 1
Inspections, Human Medicines Pharmacovigilance & Committees

EudraVigilance Go-Live Plan

Steps to be followed by national competent authorities, marketing authorisation holders and sponsors of clinical trials in the EEA

Pharmacovigilance Business Team (for consultation)	18 July – 11 August 2017 22 August 2017 28 August 2017
Clinical Trial Facilitation Group (CTFG)- Subgroup H (for consultation)	26 July – 11 August 2017
Pharmacovigilance Risk Assessment Committee (PRAC) (for consultation)	26 July – 11 August 2017 1 September 2017 14 September 2017
Pharmacovigilance Risk Assessment Committee (PRAC) (endorsement)	1 September 2017
Clinical Trial Facilitation Group (CTFG) (endorsement)	5 September 2017
EudraVigilance Expert Working Group (for consultation)	15 September 2017
IT Directors (for information)	15 September 2017
EU Telematics Management Board (EUTMB) (for information)	18 September 2017
EU Pharmacovigilance Oversight Group (EU-POG) (for information)	18 September 2017

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Table of contents

Versions

Date	Version number	Summary of changes
3 October 2017		Original document.
13 October 2017	1.0	The first revision of the document has been carried out to include a clarification on the Paul-Ehrlich Institute's adverse reaction reporting arrangements during the EudraVigilance cutover period.

1. Executive summary

The European Medicines Agency (EMA) will launch a new and improved version of EudraVigilance, the European information system of suspected adverse reactions to medicines that are authorised or being studied in clinical trials in the European Economic Area (EEA).

Following the EMA Management Board confirmation and announcement in May 2017 that the database has achieved full functionality, the new version of EudraVigilance will go live on 22 November 2017 with enhanced functionalities for reporting and analysing suspected adverse reactions. The public health benefits from the new system and operational benefits for stakeholders and regulators will provide a robust basis for pharmacovigilance and signal management activities for years to come, so it is important that care is taken in transitioning from the current to the new database.

This go-live plan outlines a set of detailed, sequenced tasks and activities required to launch the new EudraVigilance production system including the migration of more than 11 million Individual Case Safety Reports (ICSRs) and associated data and the decommissioning of the current (legacy) EudraVigilance system as regards the ICSR reporting and processing functionalities. To allow for a smooth transition from the current to the new EudraVigilance system, a cutover (downtime) period of 10 business days i.e. from 8 to 21 November 2017 is required, where key functionalities of EudraVigilance will not or only partially be available.

During the cutover period, the **electronic reporting of ICSRs** by national competent authorities (NCAs), marketing authorisation holders (MAHs) and sponsors of clinical trials (sponsors) will be **disrupted**. The **electronic submissions of data on medicines** (Article 57) will be **unavailable**.

Signal management by NCAs and EMA will be **impacted to a small extent**, as the current EVDAS will be kept operational until 21 November with a last data refresh to be performed on 7 November 2017.

The **adrreports.eu portal website will remain live**, based on the latest monthly data refresh of 31 October 2017.

The reporting by patients and healthcare professional to national competent authorities (NCAs) and marketing authorisation holders (MAHs) in the EEA will not be impacted during the cutover phase to the new EudraVigilance system.

This go-live plan further describes the stakeholders impacted and sets out the technical and business process related aspects as well as alternative arrangements for reporting of ICSRs that need to be planned for by stakeholders to ensure a successful transition. Procedures are in place for urgent reporting of important safety information and are reiterated in this go-live plan.

The Agency has carefully considered a number of options, all of which require some downtime and has selected that of 10 business days since shorter times carried higher technical risk that the process would take longer than planned and either would have to be rolled back or would risk the new system going life after 22 November 2017.

After the 22 November 2017, the current EudraVigilance System will remain operational but restricted to the functionalities related to the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) and the electronic data submission on medicines (Article 57).

2. Introduction

The European Medicines Agency (EMA) will launch a new and improved version of EudraVigilance, the European information system of suspected adverse reactions to medicines that are authorised or being studied in clinical trials in the European Economic Area (EEA). The new version of EudraVigilance will go live on 22 November 2017 with enhanced functionalities for reporting and analysing suspected adverse reactions.

An independent audit and a subsequent favourable recommendation from EMA's Pharmacovigilance Risk Assessment Committee (PRAC) concluded that the updated EudraVigilance system is fully functional. Therefore, pursuant to Article 24(2) third subparagraph of Regulation (EC) No 726/2004, EMA's Management Board confirmed and announced that the EudraVigilance database has achieved full functionality and the system meets the functional specifications. Together with the launch, further legal obligations will become applicable to the mandatory electronic reporting through EudraVigilance as stated in the announcement of the EMA Management Board.

The enhancements for reporting and analysing suspected adverse reactions of the new EudraVigilance system will support better safety monitoring of medicines and a more efficient reporting process for stakeholders. Expected benefits include:

- Simplified reporting of individual case safety reports (ICSRs) and the re-routing of ICSRs to Member States as marketing authorisation holders will no longer have to provide these reports to national competent authorities, but directly to EudraVigilance, which will ultimately reduce duplication of efforts. An ICSR provides information on an individual case of a suspected adverse reaction to a medicine;
- Better detection of new or changing safety issues, enabling rapid action to protect public health;
- Increased transparency based on broader access to reports of suspected adverse reactions by healthcare professionals and general public via the adrreports.eu portal, the public interface of the EudraVigilance database;
- Enhanced search and more efficient data analysis capabilities;
- Increased system capacity and performance to support large volumes of users and reports (including non-serious adverse reactions originating from the EEA);
- More efficient collaboration with the World Health Organization (WHO) as EMA will make the reports of individual cases of suspected adverse reactions within the EEA available to the WHO Uppsala Monitoring Centre directly from EudraVigilance; Member States will no longer need to carry out this task.

The reporting of adverse reactions by patients and healthcare professionals to national competent authorities based on local spontaneous reporting systems will remain unchanged. There will also be no changes to the reporting of suspected unexpected serious adverse reactions during clinical trials until the application of the new Clinical Trial Regulation.

Users of the system, i.e. national competent authorities, marketing authorisation holders and sponsors of clinical trials, have to make final preparations to ensure that their processes and local IT infrastructure are compatible with the new system and the internationally agreed format. A technical support plan and checklist for national Competent Authorities in the EEA as well as marketing authorisation holders and sponsors of clinical trials in support of the go-live of the enhanced EudraVigilance System were published in June 2017.

This go-live plan outlines a set of detailed, sequenced tasks and activities required to launch the new EudraVigilance production system including the migration of more than 11 million ICSRs and associated data and the decommissioning of the current (legacy) EudraVigilance system for ICSR reporting and data analysis.

In addition, it defines the stakeholders impacted and sets out the technical and business process related aspects that need to be planned for by stakeholders to ensure a successful cutover.

A successful cutover will be achieved through:

- Execution of the go-live plan with the aim of minimal impact on the daily business activities of stakeholders;
- Co-ordination of all technical and business process related changes and alternative arrangements associated with putting the new EudraVigilance system into operation;
- Execution of the go-live plan within the established timeframes.

Chart 1 outlines the key areas of activities of this go-live plan and the EudraVigilance changeover strategy. Each of the key areas is further described in the following chapters with an outline of the activities to be carried out by concerned stakeholders.

3. Stakeholders

As part of the go-live planning strategy, the following stakeholders will be impacted:

Stakeholder Group	Acronym
European Medicines Agency	EMA
National Competent Authorities in the European Economic Area	NCAs
Marketing Authorisation Holders	MAHs
General public	Public
Sponsors of clinical trials	Sponsors
World Health Organisation - Uppsala Monitoring Center	WHO-UMC

ID	Task Name	Start	Finish	Duration
1	EudraVigilance pre-cutover activities	15/09/2017	22/01/2018	92d
2	EudraVigilance cutover activities	08/11/2017	21/11/2017	10d
3	EudraVigilance go-live	22/11/2017	22/11/2017	0d
4	EudraVigilance cutover legacy	22/11/2017	24/11/2017	3d
5	EudraVigilance post-go-live	22/11/2017	22/11/2017	0d

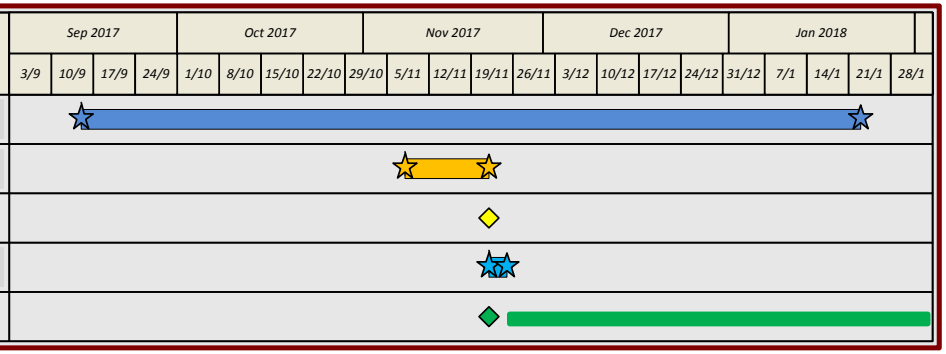


Chart 1: Key areas of activities of this go-live plan and the EudraVigilance changeover strategy (Note: duration is indicated in business days excluding weekends)

4. EudraVigilance pre-cutover activities

Prior to the initiation of the EudraVigilance cutover period, the present business processes related to the use of the current EudraVigilance system will continue as is. Testing activities with the new EudraVigilance XCOMP (test) environments can also continue with the exception of the 18 to 20 September 2017 and the week of 23 to 27 October 2017. The Gateway will not be available on 23 September 2017 due to software upgrades. The activities as part of the EudraVigilance pre-cutover phase and associated timelines are summarised in chart 2 and are further outlined below.

4.1. *ADR reporting (pharmacovigilance) – interim arrangements*

Prior to the initiation of the EudraVigilance cutover period the following applies:

- NCAs and MAHs in the EEA report suspected adverse reactions in accordance with the presently applied interim arrangements as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products **(Rev 1)**, chapter VI.C.4.1. *Interim arrangements apply* (see also Appendix 3 Modalities for reporting);
- NCAs in the EEA provide reports of suspected adverse reactions to the WHO (see also Appendix 4 of GVP Module VI, *Rev 1*, *Transmission of ICSRs to World Health Organization (WHO)*).

4.2. *SUSAR reporting – clinical trials*

Prior to the initiation of the EudraVigilance cutover period the following applies:

- Sponsors report suspected unexpected serious adverse reactions (SUSARs) for clinical trials in accordance with the present arrangements and based on the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01).

4.3. *Medical literature monitoring (MLM) by the Agency*

Prior to the initiation of the EudraVigilance cutover period the following applies:

- EMA operates the medical literature monitoring (MLM) service in accordance with Article 27 of Regulation (EC) No 726/2004.

4.4. *Data submission on medicines to the XEVMPD*

- Prior to the initiation of the EudraVigilance cutover period the following applies:
- MAHs submit data on medicines using the XEVMPD and keep this information up-to-date in accordance with Article 57 of Regulation (EC) No 726/2004.

4.5. *Signal management NCAs and EMA*

Prior to the initiation of the EudraVigilance cutover period the following applies:

- EMA and NCAs in the EEA perform signal management in accordance with (GVP) Module IX – Signal management.

4.6. *EudraVigilance registration of organisation / users*

Prior to the initiation of the EudraVigilance cutover period the following applies:

- The registration process of new organisations and users (new users and updates) continues in accordance with the established registration process and the phased EVDAS registration schedule as described at the EudraVigilance: how to register webpage.

4.7. *Interoperability testing with the new EudraVigilance XCOMP (test) environment*

Prior to the initiation of the EudraVigilance cutover period, organisations which have electronic submissions of ICSRs to EudraVigilance established, should perform the gateway configuration and communication testing with XCOMP (refer to the EU ICSR Implementation Guide).

- Organisations that will continue to use established E2B(R2) systems should use the E2B(R3) test files available for download from the external compliance testing environment (XCOMP) and test the upload of the files in their local pharmacovigilance/safety system with a backwards-and-forwards conversion solution.
- Organisations should refer to the following documents in support of their testing activities:
  - EudraVigilance technical support plan for national competent authorities in the EEA
  - EudraVigilance checklist for national competent authorities in the EEA
  - EudraVigilance testing instructions and checklist for marketing authorisation holders and sponsors of clinical trials in the EEA
- Organisations should only contact the Agency if they encounter difficulties with the testing.
- Organisations *preparing for electronic transmissions of ICSRs to EudraVigilance for the first time* or *performing major upgrades to established systems* should consult the EudraVigilance: electronic reporting webpage.

- XCOMP will not be available for testing on 18, 19 and 20 September 2017; this applies to the gateway and EVWEB system components of the XCOMP environment. Any ICSR data submitted previously into the EudraVigilance XCOMP test environment will be deleted by EMA.
- XCOMP will not be available for testing during the week of 23 to 27 October 2017.
- The Gateway will not be available on 23 September 2017 due to software upgrades.

4.8. *Adrreports.eu portal*

Prior to the initiation of the EudraVigilance cutover period, the public can access information on suspected adverse reactions related to medicines at the adrreports.eu portal. EMA will regularly update the data as per the current process.

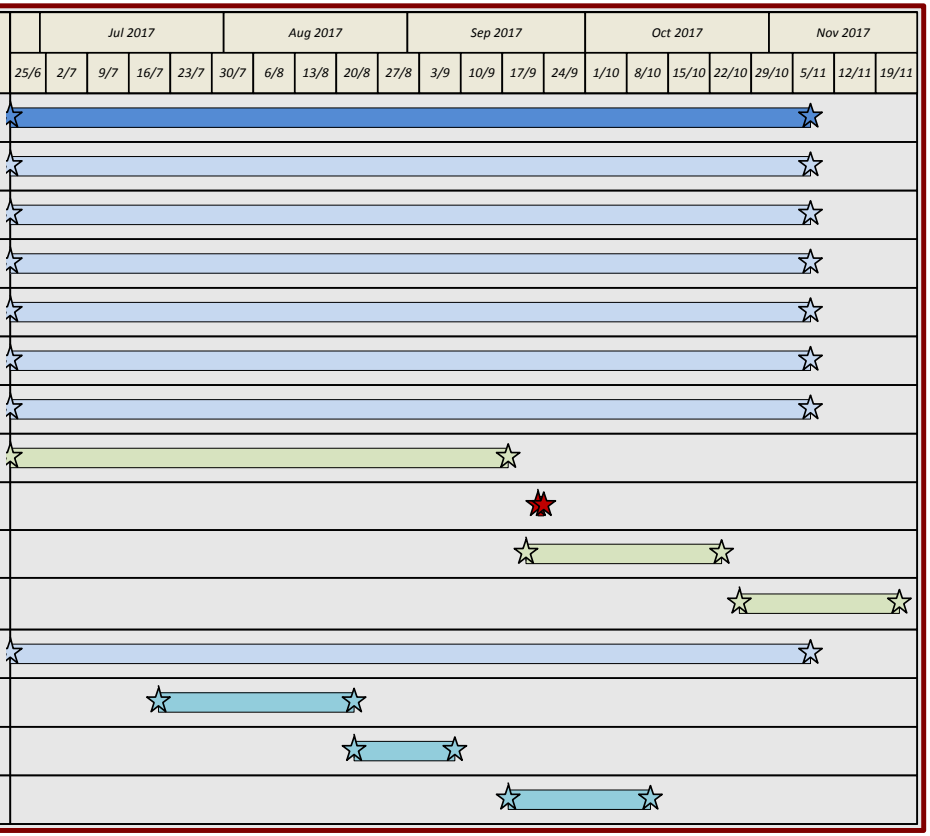
4.9. *EudraVigilance go-live rehearsal by EMA*

The go-live rehearsal (mock cutover) is utilised by the EMA to practice and validate the technical aspects of the internal go-live plan prior to the launch of the new EudraVigilance system on 22 November 2017.

It is a way of fine-tuning the process and of minimising the risks prior to full production cutover. EMA will test the launch of the new system and ensure that controls are in place by applying milestones and decision points that will drive a successful outcome of the rehearsal.

Chart 2: EudraVigilance pre-cutover period and key activities (Note: duration is indicated in calendar days)

ID	Task Name	Start	Finish	Duration
1	EudraVigilance pre-cutover period	26/06/2017	07/11/2017	135d
2	ADR reporting - Interim arrangements	26/06/2017	07/11/2017	135d
3	SUSAR reporting for clinical trials by sponsors	26/06/2017	07/11/2017	135d
4	Medical literature monitoring by EMA	26/06/2017	07/11/2017	135d
5	Data submission on medicines (Art 57)	26/06/2017	07/11/2017	135d
6	Signal management by EMA and NCAs	26/06/2017	07/11/2017	135d
7	EudraVigilance registration of organisations and users	26/06/2017	07/11/2017	135d
8	EV XCOMP interoperability testing by stakeholders	26/06/2017	17/09/2017	84d
9	Gateway software upgrade – planned gateway downtime	23/09/2017	23/09/2017	1d
10	EV XCOMP interoperability testing by stakeholders	21/09/2017	23/10/2017	33d
11	EV XCOMP interoperability testing by stakeholders	27/10/2017	22/11/2017	27d
12	Adrreports.eu portal – data aggregation/ publication	26/06/2017	07/11/2017	135d
13	EV Go-live rehearsal by EMA (1)	21/07/2017	22/08/2017	33d
14	EV Go-live rehearsal by EMA (2)	23/08/2017	08/09/2017	17d
15	EV Go-live rehearsal by EMA (3)	18/09/2017	11/10/2017	24d



5. EudraVigilance cutover activities

For the successful cutover from the current to the new EudraVigilance system, integrated system and business transition activities will need to be performed that subsequently will also impact stakeholders. In practice this implies that some of the current EudraVigilance system components will not be available for a defined period of time so that the new EudraVigilance system production environment components can be activated and the current legacy data of more than 11 million ICSRs can be migrated.

The business processes that are impacted by the cutover period and associated timelines are presented in chart 3.

ID	Task Name	Start	Finish	Duration	Nov 2017
					5/11 12/11 19/11
1	EudraVigilance cutover period	08/11/2017	21/11/2017	10d	
2	ADR reporting - alternative arrangements	08/11/2017	21/11/2017	10d	
3	SUSAR reporting for clinical trials by sponsors -alternative arrangements	08/11/2017	21/11/2017	10d	
4	Medical literature monitoring by EMA – partial service	08/11/2017	21/11/2017	10d	
5	Data submission on medicines (Art 57) - unavailable	08/11/2017	21/11/2017	10d	
6	Signal management by EMA and NCAs – minor impact	08/11/2017	21/11/2017	10d	
7	EudraVigilance registration of organisations and users – not available	08/11/2017	21/11/2017	10d	
8	Adrreports.eu portal -data aggregation/ publication – no impact	08/11/2017	21/11/2017	10d	
9	EV XCOMP interoperability testing by stakeholders – no impact	08/11/2017	21/11/2017	10d	

Chart 3: Activities impacted by the cutover period and associated timelines (Note: duration is indicated in business days excluding weekends)

The cut-over activities for the transition from the current to the new EudraVigilance system will start on the 8 November 2017 at 00:00 a.m. UK time and will end on 22 November 2017 at 9:00 a.m. UK time.

The EudraVigilance system components, their availability during the cutover, the impacted stakeholders and business processes are summarised in Table 1.

Table 1. Summary of EudraVigilance system components and impact of downtime

EudraVigilance System component	Availability during cutover	Stakeholder impacted	Business processes impacted
EudraVigilance Gateway	Partially available 	NCAs, MAHs, sponsors, EMA	ADR reporting, SUSAR reporting, data submission on medicines
WEBTRADER: EVWEB and EVPOST functions	**Unavailable** 	NCAs, MAHs, sponsors, EMA	Electronic submission of ICSRs (pre and post authorisation), electronic submission of on medicines
EVWEB	**Unavailable** 	NCAs, MAHs, sponsors, EMA	ADR reporting, SUSAR reporting, MLM service ICSR generation, data submission on medicines
EudraVigilance restricted area	**Unavailable** 	NCAs, MAHs, sponsors, EMA	Access to information on Organisation IDs; user privilege updates; access to MLM service tracking sheets
EudraVigilance Registration application	**Unavailable** 	NCAs, MAHs, sponsors, EMA	Registration of organisation and users
EudraVigilance Database Management System (EVDBMS)	**Unavailable** 	NCAs, MAHs, sponsors, EMA	Business rule validation, ICSR processing, re-coding, duplicate management, ETL for EVDAS
EVDAS, eRMRs	**Available** 	NCAs, EMA	Signal management (last data refresh on 7 November 2017)
Addreports.eu portal	**Available** 	Public	Access to ADRs by patients and healthcare professionals (last data refresh based on present monthly schedule)

An overview of the business processes that are supported/not supported based on the availability of the EudraVigilance system components during the cutover period as well as the alternative arrangements that should be followed by stakeholders are reflected in Table 2 and further described in chapters 5.1. to 5.7.

Table 2. Overview of the processes that are supported and not supported during the cutover period and alternative arrangements that should be followed

ID	EudraVigilance System component	Availability during downtime	Stakeholder impacted	Process supported during cutover	Process NOT supported during cutover	Alternative arrangements during cutover
a.	**EudraVigilance Gateway** ***ICSR submissions***	**Partial available** 	NCAs, MAHs, sponsors, EMA	• **Electronic submissions of ICSRs (safety) and ACK messages:** – **Gateway organisation to gateway organisation** • **MDNs will be generated**	• **XML / business rule validation will not be supported**	See reporting options as described in chapter 5.1 and 5.2.
b.	**EudraVigilance Gateway** **WEBTRADER: EVWEB and EVPOST functions** **ICSR submissions**	**Partial available** 	**NCAs, MAHs, sponsors, EMA**	• **Electronic submissions of ICSRs (safety) and ACK messages between:** – **Gateway organisation to WEBTRADER organisation** • **MDNs will be generated**	• **For submissions to WEBTRADER organisations, ACKs will not be generated.** • **ACKs will only be returned once the new EudraVigilance production environment goes live and WEBTRADER organisations have generated ACK**	**Gateway organisations must stop the process of re-submitting safety messages to WEBTRADER organisations for which after 48 hours no ACKs have been received.** See reporting options as described in chapter 5.1

ID	EudraVigilance System component	Availability during downtime	Stakeholder impacted	Process supported during cutover	Process NOT supported during cutover	Alternative arrangements during cutover
					messages.	and 5.2.
c.	**EudraVigilance Gateway** ***ICSR submissions***	**Not available**	NCAs, MAHs, sponsors, EMA	**Not applicable**	• No electronic submissions of ICSRs (safety) and ACK messages: – **Gateway organisation to EudraVigilance (EVPM and EVCTM)**	The sender organisation must submit valid ICH E2B(R2) or ICH E2B(R3) safety messages to EudraVigilance (EVPM or EVCTM as applicable) when the gateway of the new EudraVigilance system is going live. See reporting options as described in chapter 5.1 and 5.2.
d.	**WEBTRADER: EVWEB and EVPOST functions** ***ICSR submissions***	**Unavailable**	NCAs, MAHs, sponsors, EMA	None	• No electronic submissions of ICSRs (safety) and ACK messages possible by: – Gateway organisation to EudraVigilance (EVPM and EVCTM) – WEBTRADER organisations to EudraVigilance (EVPM and EVCTM)	The sender organisation must submit valid ICH E2B(R2) or ICH E2B(R3) safety messages to EudraVigilance (EVPM or EVCTM as applicable) when the gateway of the new EudraVigilance system is going live. See reporting options as described in chapter 5.1

ID	EudraVigilance System component	Availability during downtime	Stakeholder impacted	Process supported during cutover	Process NOT supported during cutover	Alternative arrangements during cutover
						and 5.2.
e.	**WEBTRADER: EVWEB and EVPOST functions)** ***Data on medicines submissions***	**Unavailable**	MAHs, sponsors, EMA	None	• No electronic submissions of data on medicines (Art 57) are possible. This applies to: – Gateway organisation to XEVMPD – WEBTRADER organisation to XEVMPD	See reporting options as described in chapter 5.1 and 5.2.
f.	**EudraVigilance Restricted Area**	**Unavailable**	NCAs, MAHs, sponsors of clinical trials, EMA	None	• Access to information provided in the restricted area of EudraVigilance i.e. Organisation Identifiers in support of the EDI process; MLM tracking sheets	None
g.	**EVWEB** (incl. MLM ICSR Export Manager)	**Unavailable**	NCAs, MAHs, sponsors, EMA	None	• No electronic submissions of ICSRs (safety) and ACK messages. • No receipt of safety and acknowledgement messages possible • Accessing and download	The sender organisation must submit valid ICH E2B(R2) or ICH E2B(R3) safety messages to EudraVigilance (EVPM or EVCTM as applicable) when the gateway of the new EudraVigilance is

ID	EudraVigilance System component	Availability during downtime	Stakeholder impacted	Process supported during cutover	Process NOT supported during cutover	Alternative arrangements during cutover
					MLM cases not possible	going live. See reporting options as described in chapter 5.1 and 5.2.
h.	**EVDBMS**	**Unavailable**	NCAs, MAHs, sponsors, EMA	None	• Processing of safety and ACK messages, EVPRMs, business rules validation, recoding and duplicate detection will not be supported	None
i.	**EVDAS**	**Available**	NCAs, EMA	Signal management will be supported based on the data with a cut-off date of 07 November 2017	• The ETL will not run and therefore no initial, follow-up or nullification reports or master cases will be transferred into EVDAS • Additional eRMR for the 15 November (reference period 23 October to 12 November 2017) will not be produced	The signal management activities will continue as per normal process by NCAs and EMAs (**with data lock point of 7 November 2017**) Note: the hyperlinks in the eRMRs produced until 7 November 2017 will be working until 21 November 2017; eRMRs produced after that date will contain hyperlinks for

ID	EudraVigilance System component	Availability during downtime	Stakeholder impacted	Process supported during cutover	Process NOT supported during cutover	Alternative arrangements during cutover
						the new EVDAS
j.	**Adrreports.eu portal**	✓	Public	Access to aggregated ADR data from EudraVigilance will be provided with the cut-off date of 31 October 2017 as per normal process.	N/A	None

5.1. *ADR reporting (pharmacovigilance)*

During the EudraVigilance cutover period, the reporting options as described in chapters 5.1.1. to 5.1.3. The time specified in the tables below refers to local time.

- **Events/observations identified during the cutover date, which may affect the risk-benefit balance of a medicinal product, should be notified as emerging safety issue in accordance with** GVP Module VI, **revision 1**, chapter VI.C.2.2.6. Emerging safety issues.
- With EVPM not being available as of 8 November 2017, the sender organisation needs to be aware that acknowledgement messages (ACKs) for safety messages sent on 6 and 7 November, may not be returned. This is due to the fact that ACKs may take up to 48 hours to be generated and returned by the receiver organisation by means of the EudraVigilance Gateway. Where no ACKs are received by the sender organisation for messages sent as of 6 November 2017, the message disposition notification (MDN) should serve as confirmation of the delivery of the message to the receiver organisation. **This is on the basis that the safety messages submitted were valid and did not contain errors.**

- **Safety messages must NOT be submitted to EVPM during the cutover period.**
- **The safety messages will NOT be queued and will be discarded.**

5.1.1. ADR reporting - option 1 during cutover period

During the cutover period, the sender organisation (NCA/MAH) stops the submission of ICSRs (see figure 1).

This applies for the submission of ICSRs from:

- an NCA to an MAH;
- an MAH to an NCA;
- an NCA to EVPM;
- an MAH to EVPM;
- an NCA to WHO UMC.

These reports are to be submitted electronically by the NCA/the MAH to EVPM as part of the cutover legacy /post-go-live period **in accordance with the simplified reporting rules** as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products **(Revision 2)** as of 22 November 2017 (see chapter 6.1).

These reports will be made available to NCAs/MAHs and WHO-UMC as part of the cutover legacy/post-go-live period in accordance with the simplified reporting rules (see chapter 6.1).

No alternative arrangements for reporting by a MAH to a NCA apply during the cutover period.

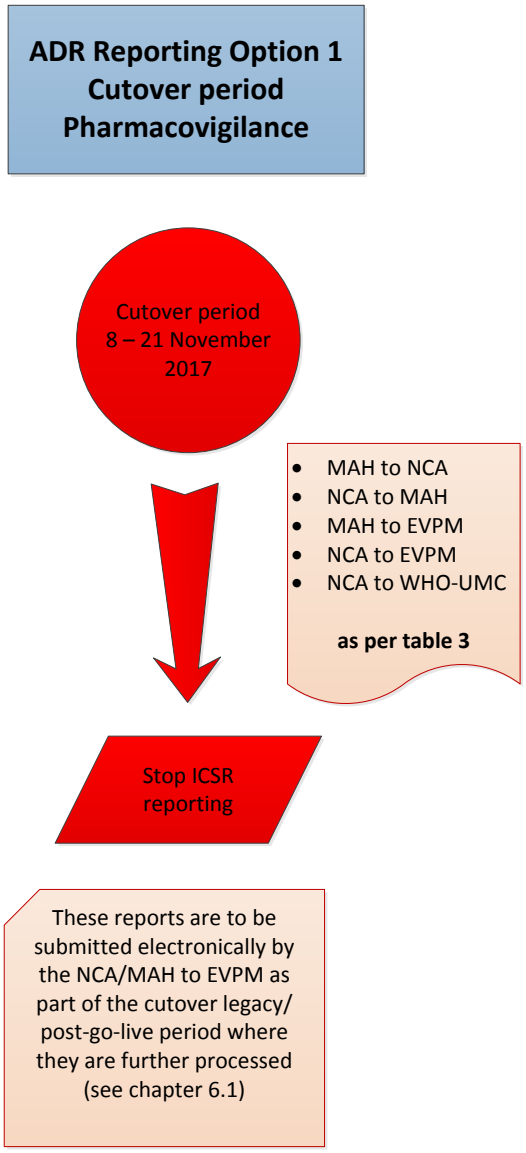


Figure 1: ADR reporting Option 1 during cutover period

Option 1 applies to the NCAs as reflected in Table 3.

Table 3: NCAs for which ADR reporting according to option 1 during the cutover period applies

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
BASG - Bundesamt für Sicherheit im Gesundheitswesen	AT	1	The Austrian Agency (HQ ORG-ID BDA) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Austrian Agency (HQ ORG-ID BDA) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Austrian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten - Agence Fédérale des Médicaments et des Produits de Santé	BE	1	The Belgian Agency (HQ ORG-ID AFIGP) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Belgian Agency (ORG-ID AFIGP) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Belgian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Bulgarian Drug Agency – Ministry of Health	BG	1	The Bulgarian Agency (HQ ORG-ID BDA) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Bulgarian Agency (HQ ORG-ID BDA) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Bulgarian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Ministry of Health – Pharmaceutical Services	CY	1	The Ministry of Health in Cyprus (HQ ORG-ID CYPPVPR) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Ministry of Health in Cyprus (HQ ORG-ID CYPPVPR) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Ministry of Health in Cyprus will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
Ravimiamet	EE	1	The Estonian Agency (HQ ORG-ID SAM) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Estonian Agency (HQ ORG-ID SAM) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Estonian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Agencia Española de Medicamentos y Productos Sanitarios	ES	1	The Spanish Agency AEMPS (HQ ORG-ID AGEMED) will stop receiving ICSRs from MAHs as of 6 (00:00) November 2017. Any ICSRs from 6 and 7 November should be submitted by MAHs to EVPM after 22 November along with the other cutover legacy ICSRs. The Spanish Agency AEMPS (HQ ORG-ID AGEMED) will stop sending ICSRs to MAHs as of 6 (00:00) November 2017. The Spanish Agency AEMPS will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Lääkealan turvallisuus- ja kehittämiskeskus	FI	1	The Finish Agency (HQ ORG-ID FINAM) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Finish Agency (HQ ORG-ID FINAM) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Finish Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
Agence nationale de sécurité du médicament et des produits de santé	FR	1	The French Agency ANSM (HQ ORG-ID AFSSAPS) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The French Agency ANSM (HQ ORG-ID AFSSAPS) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The French Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Agencija za Lijekove i Medicinske Proizvode	HR	1	The Croatian Agency HALMED (HQ ORG-ID ALMP) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Croatian Agency HALMED (HQ ORG-ID ALMP) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Croatian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Health Products Regulatory Authority/An tÚdarás Rialála Táirgí Sláinte	IE	1	The Irish Agency **HPRA (HQ ORG-ID IMB) will stop receiving ICSRs from MAHs as of 4 (00:00) November 2017.** Any ICSRs from 4-7 November should be submitted by MAHs to EVPM after 22 November along with the other cutover legacy ICSRs. The Irish Agency **HPRA (HQ ORG-ID IMB) will stop sending ICSRs to MAHs as of 4 (00:00) November 2017.** The Irish Agency HPRA will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
Office of Health / Medicinal Products Control Agency	LI	1	The Liechtenstein Agency (HQ ORG-ID KARZNEI) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Liechtenstein Agency (HQ ORG-ID KARZNEI) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Liechtenstein Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Ministère de la Santé	LU	1	The Luxemburg Agency (HQ ORG-ID DPM) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Luxemburg Agency (HQ ORG-ID DPM) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Luxemburg Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Valstybinė vaistų kontrolės tarnyba prie Lietuvos Respublikos sveikatos apsaugos ministerijos	LT	1	The Lithuanian Agency (HQ ORG-ID SMCAP) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Lithuanian Agency (HQ ORG-ID SMCAP) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Lithuanian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.The Lithuanian Agency (HQ ORG-ID SMCAP) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017.

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
Zāļu valsts aģentūra	LV	1	The Latvian Agency (HQ ORG-IDLRZBP2005) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Latvian Agency (HQ ORG-ID LRZBP2005) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Latvian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Awtorità dwar il-Mediċini	MT	1	The Maltese Agency (HQ ORG-ID ADM) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Maltese Agency (HQ ORG-ID ADM) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Maltese Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
College ter Beoordeling van Geneesmiddelen	NL	1	The Dutch Agency MEB (HQ ORG-ID (CBGMEB) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Dutch Agency MEB (HQ ORG-ID (CBGMEB) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Dutch Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Statens legemiddelverk	NO	1	The Norwegian Agency (HQ ORG-ID NOMAADVRE) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Norwegian Agency (HQ ORG-ID NOMAADVRE) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Norwegian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
Urząd Rejestracji Produktów Leczniczych, Wyrobow Medycznych i Produktów Biobójczych	PL	1	The Polish Agency (HQ ORG-ID URPL) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Polish Agency (HQ ORG-ID URPL) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Polish Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
INFARMED - Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.	PT	1	The Portuguese Agency (HQ ORG-ID INFARMED) will stop receiving ICSRs from MAHs as of 7 (00:00) November 2017. The Portuguese Agency (HQ ORG-ID INFARMED) will stop sending ICSRs to MAHs as of 7 (00:00) November 2017. The Portuguese Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Läkemedelsverket	SE	1	The Swedish Agency (HQ ORG-ID SEMPA) should not receive ICSRs from MAHs according to the current practice. The Swedish Agency (HQ ORG-ID SEMPA) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Swedish Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
Javna agencija Republike Slovenije za zdravila in medicinske pripomočke	SI	1	The Slovenian Agency (HQ ORG-ID ARSZMP) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Slovenian Agency (HQ ORG-ID ARSZMP) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Slovenian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
Štátny ústav pre kontrolu liečiv	SK	1	The Slovakian Agency (HQ ORG-ID SUKLSK) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Slovakian Agency (HQ ORG-ID SUKLSK) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Slovakian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
EudraVigilance Post-Authorisation Module (EVPM)	EU	1	EVPM will stop receiving ICSRs from NCAs and MAHs as of 8 (00:00) November 2017.

5.1.2. ADR reporting - option 2 during cutover period

During the cutover period, the sender organisation (NCA / MAH) stops the submission of ICSRs (see figure 2)**.**

This applies for the submission of ICSRs from:

- an NCA to an MAH;
- an MAH to an NCA;
- an NCA to EVPM;
- an MAH to EVPM;
- an NCA to WHO UMC.

These reports are to be submitted electronically by the NCA/the MAH to EVPM as part of the cutover legacy /post-go-live period **in accordance with the simplified reporting rules** as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products **(Revision 2)** as of 22 November 2017 (see chapter 6.1).

These reports will be made available to NCAs/MAHs and WHO-UMC as part of the cutover legacy/post-go-live period in accordance with the simplified reporting rules (see chapter 6.1).

In addition, the MAH has to follow alternative arrangements for the adverse reaction reporting to the NCA during the cutover period based on one of the following principles:

A. The MAH generates with their local system valid safety message(s) **an XML and CIOMS I format** and submits the cases via e-mail to the NCA. The MAH writes "**ADR reporting - Failure of safety message generation at receiver's side**" on the paper report(s)/ CIOMS forms (pdf) and states in the email/cover letter subject: "**ADR reporting cutover period**".

B. The MAH sends case report(s) in an internationally acknowledged format (CIOMS I) to a dedicated fax line (in paper format), to a dedicated e-mail (in pdf format) or via post (in paper

format) to the NCA and writes "**ADR reporting - Failure of safety message generation at receiver's side**" on the paper report(s)/email/letter.

C. The MAH follows dedicated national reporting arrangements.

As part of the alternative arrangements, the MAH reports suspected adverse reactions **in accordance with the current interim reporting provisions** as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products **(Revision 1)**, chapter VI.C.4.1. Interim arrangements apply (see also Appendix 3 Modalities for reporting).

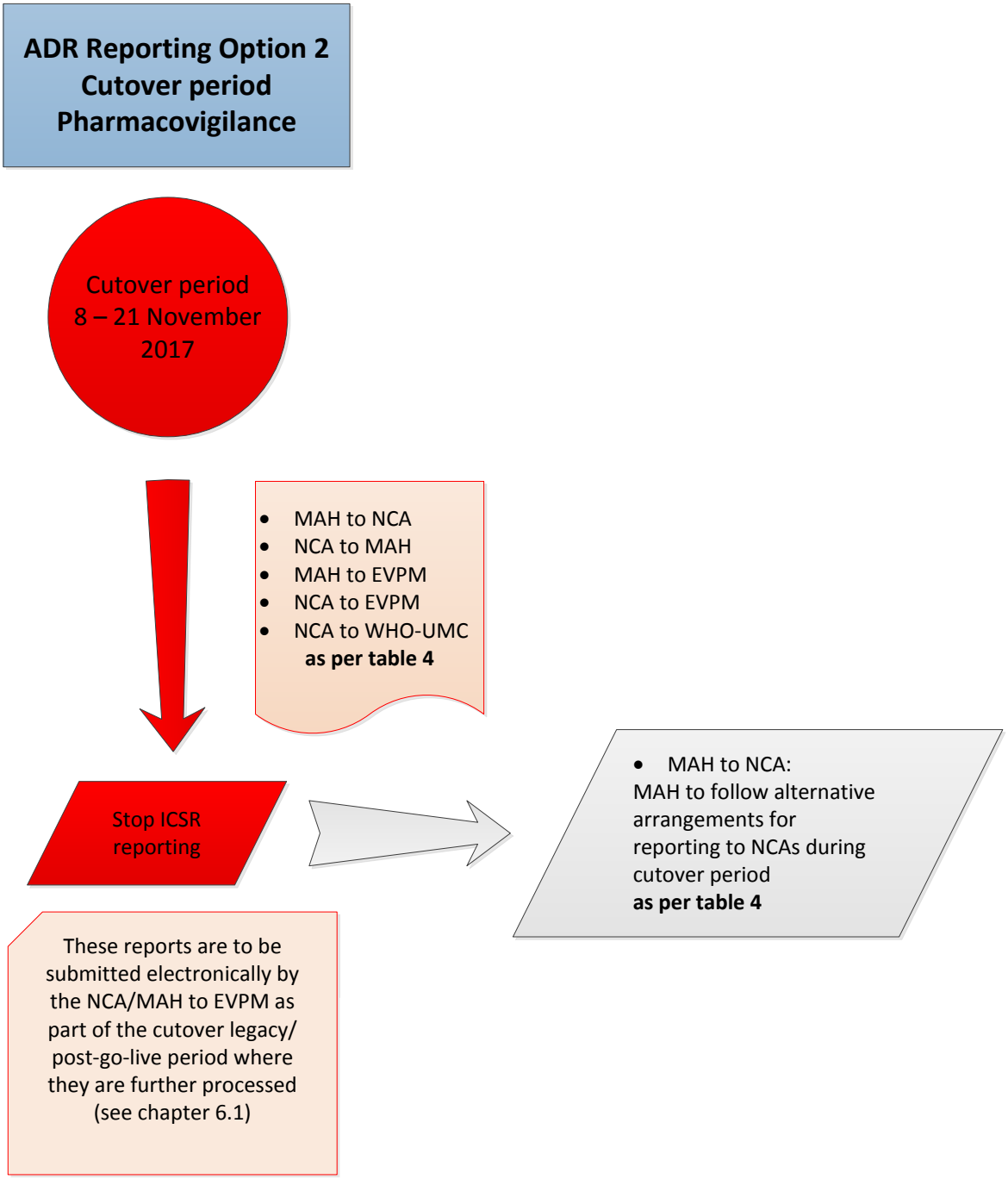


Figure 2: ADR reporting Option 1B during cutover period

Option 2 applies to NCAs as reflected in Table 4.

Table 4: NCAs for which ADR reporting according to option 2 during the cutover period applies

National Competent Authority / EudraVigilance	Member State	Option	Alternative arrangements
Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet	HU	2A	The Hungarian Agency OGYEI (HQ ORG-ID OGYIP) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Hungarian Agency (HQ ORG-ID OGYIP) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Hungarian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017. **From 8 to 21 November**, **serious ICSRs** concerning Hungary from MAHs should be submitted to OGYEI in XML and CIOMS I format via email to adr.box@ogyei.gov.hu For MAHs which cannot generate XMLs, submission in CIOMS I format only will be accepted. OGYEI will acknowledge the receipt of cases via a reply to these emails within 2 business days. Since no ICSR Message Disposition Notification (MDN) is generated in this process for the files provided by email, the date of dispatch of the report via email is sufficient to prove regulatory compliance.
Státní ústav pro kontrolu léčiv	CZ	2B	The Czech Agency (HQ ORG-ID CZSUKL) will stop receiving ICSRs from MAHs as of 7 (00:00) November 2017. The Czech Agency (HQ ORG-ID CZSUKL) will stop sending ICSRs to MAHs as of 7 (00:00) November 2017. The Czech Agency will stop sending ICSRs to WHO UMC as of 7 (00:00) November 2017. **From 7 (00:00) to 21 (24:00) November 2017**, MAHs have to report individual cases originating from the Czech Republic in CIOMS I format to the following dedicated email address: farmakovigilance@sukl.cz

National Competent Authority / EudraVigilance	Member State	Option	Alternative arrangements
Danish Medicines Agency	DK	2B	The Danish Agency DKMA (HQ ORG-ID DKMAEUDRA) will stop receiving ICSRs from MAHs **as of 6 (12:00 CET) November 2017**. The Danish Agency DKMA (HQ ORG-ID DKMAEUDRA) will stop sending ICSRs to MAHs **as of 8 (00:00) November 2017**. The Danish Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017. Individual cases that MAHs wish to submit during the cutover period of 6 to 21 November should be faxed in CIOMS I format using the following dedicated fax line: +45 44889599 *(CIOM I forms should only be submitted by fax if patient safety might be compromised and it is judged by the sender that reporting cannot wait).* Danish legislation concerning sensitive personal information does not allow transmission via un-encrypted e-mail. Any ICSRs from 6 (12:00 CET) and 7 November should be submitted by MAHs to EVPM after 22 November along with the other cutover legacy ICSRs.

National Competent Authority / EudraVigilance	Member State	Option	Alternative arrangements
National Organization for Medicines	GR	2B	The Greek Agency (HQ ORG-ID GREOF) will stop receiving ICSRs from MAHs **as of 6 (00:00) November 2017**. The Greek Agency (HQ ORG-ID GREOF) will stop sending ICSRs to MAHs **as of 6 (00:00) November 2017**. The Greek Agency will stop sending ICSRs to WHO UMC as of 6 (00:00) November 2017. **From 7 (00:00) to 21 (24:00) November 2017**, MAHs have to report individual cases originating from Greece in CIOMS I format to the Greek Agency as follows: Email: ev@eof.gr (pdf format) or Fax: +30 210 6549585 indicating "ICSR" in the email/fax cover subject. Any ICSRs from 6 and 7 November should be submitted by MAHs to EVPM after 22 November along with the other cutover legacy ICSRs.
Lyfjastofnun	IS	2C	The Islandic Agency (HQ ORG-ID ADALIMCA01) will stop receiving ICSRs from MAHs as of 8 (00:00) November 2017. The Islandic Agency (HQ ORG-ID ADALIMCA01) will stop sending ICSRs to MAHs as of 8 (00:00) November 2017. The Islandic Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017. **From 8 (00:00) to 21 (24:00) November 2017**, MAHs have to report individual cases originating from Island using the IMAS web portal.

National Competent Authority / EudraVigilance	Member State	Option	Alternative arrangements
Agentia Naţională a Medicamentului şi a Dispozitivelor Medicale	RO	2B	The Romanian Agency (HQ ORG-ID NMA) will stop receiving ICSRs from MAHs **as of 7 (00:00) November 2017**. The Romanian Agency (HQ ORG-ID NMA) will stop sending ICSRs to MAHs **as of 7 (00:00) November 2017**. The Romanian Agency will stop sending ICSRs to WHO UMC as of 7 (00:00) November 2017. **From 7 (00:00) to 21 (24:00) November 2017**, MAHs have to report individual cases originating from the Romania in CIOMS I format to: Email: farmacovigilenta@anm.ro Any ICSRs from 7 November should be submitted by MAHs to EVPM after 22 November along with the other cutover legacy ICSRs.
Agenzia Italiana del Farmaco	IT	2C	Until 21 (24:00) November 2017, AIFA will continue to receive the cases directly in their national pharmacovigilance database (NPhVD) as foreseen by the transitional (interim) reporting measures set out in GVP Module VI revision 1. At the moment AIFA doesn't receive directly the cases originating from IT from the MAHs but these cases are processed by the responsible of pharmacovigilance (RPhV) of the local structure to which the reporter belongs. For reference: http://www.agenziafarmaco.gov.it/it/responsabili. If a MAH receives directly a case from a reporter, this report should be sent only to the local RPhV for the data entry in the NPhVD. The other reporters (doctor, pharmacist, nurse, patient, etc….) should send the reports to the RPhV of the local structure to which they belong. The RPhV is the user responsible for the data entry process in the NPhVD. Generally MAHs

National Competent Authority / EudraVigilance	Member State	Option	Alternative arrangements
			become aware of a new ADR report through the NPhVD and, in particular, through a dedicated, closed electronic e-mail system, (accessible by authorised users only) by which an automatic message is generated for every input or any update of the report. If the MAH doesn't know the local structure to which the reporter belongs, it has to register the case in the NPhVD. The online reporting modality has also been made available to the public at this link: www.vigifarmaco.it. After validation by the RPhV the cases registered in the vigifarmaco are uploaded in NPhVD. After the cutover period, AIFA will send all cases registered in the NPhVD from 8-21 November directly to EudraVigilance within the 2 business days. For AIFA the new simplified reporting rules will be applied from 22 November 2017. The Italian Agency will stop sending ICSRs to WHO UMC as of 8 (00:00) November 2017.
EudraVigilance Post-Authorisation Module (EVPM)	EU	1	EVPM will stop receiving ICSRs from NCAs and MAHs as of 8 (00:00) November 2017.

5.1.3. ADR reporting - option 3 during cutover period

During the cutover period (see figure 3):

- the sender organisation (MAH) continues with the electronic submission of ICSRs to the receiver organisation (NCA) **where this is technically feasible** in accordance with table 2;
- the sender organisation (NCA) continues with the provision of ICSRs to the receiver organisation (WHO-UMC).

For these activities, the reporting of suspected adverse reactions is to be based on the **current interim reporting provisions** as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products **(Revision 1)**, chapter VI.C.4.1. Interim arrangements apply (see also Appendix 3 Modalities for reporting).

Where during the cutover period the **electronic reporting is NOT feasible**, the sender organisation (NCA/MAH) proceeds as follows:

A. Reports that cannot be submitted electronically during the cutover period of 8 (0:00) to 21 (24:00) period by the sender organisation (MAH) to the receiver organisation (NCA/EVPM),have to be submitted electronically to EVPM by the sender organisation (MAH) as part of the cutover legacy /post-go-live period **in accordance with the simplified reporting rules** as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products **(Revision 2)** as of 22 November 2017 (see chapter 6.1);

B. The MAH follows dedicated national reporting arrangements in accordance with as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products (Revision 1), chapter VI.C.4.1. Interim arrangements apply (see also Appendix 3 Modalities for reporting).

Reports that cannot be submitted electronically during the cutover period of 8 (0:00) to 21 (24:00) period by the sender organisation (MAH/NCA) to the receiver organisation (EVPM), have to be submitted electronically to EVPM by the sender organisation (MAH/NCA) as part of the cutover legacy /post-go-live period **in accordance with the simplified reporting rules** as set out in the Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products **(Revision 2)** as of 22 November 2017 (see chapter 6.1).

During the cutover period (figure 3):

- the sender organisation (MAH) stops the electronic submission of ICSRs to EVPM in accordance with table 2;
- the sender organisation (NCA) stops the electronic submission of ICSRs to EVPM in accordance with table 2.

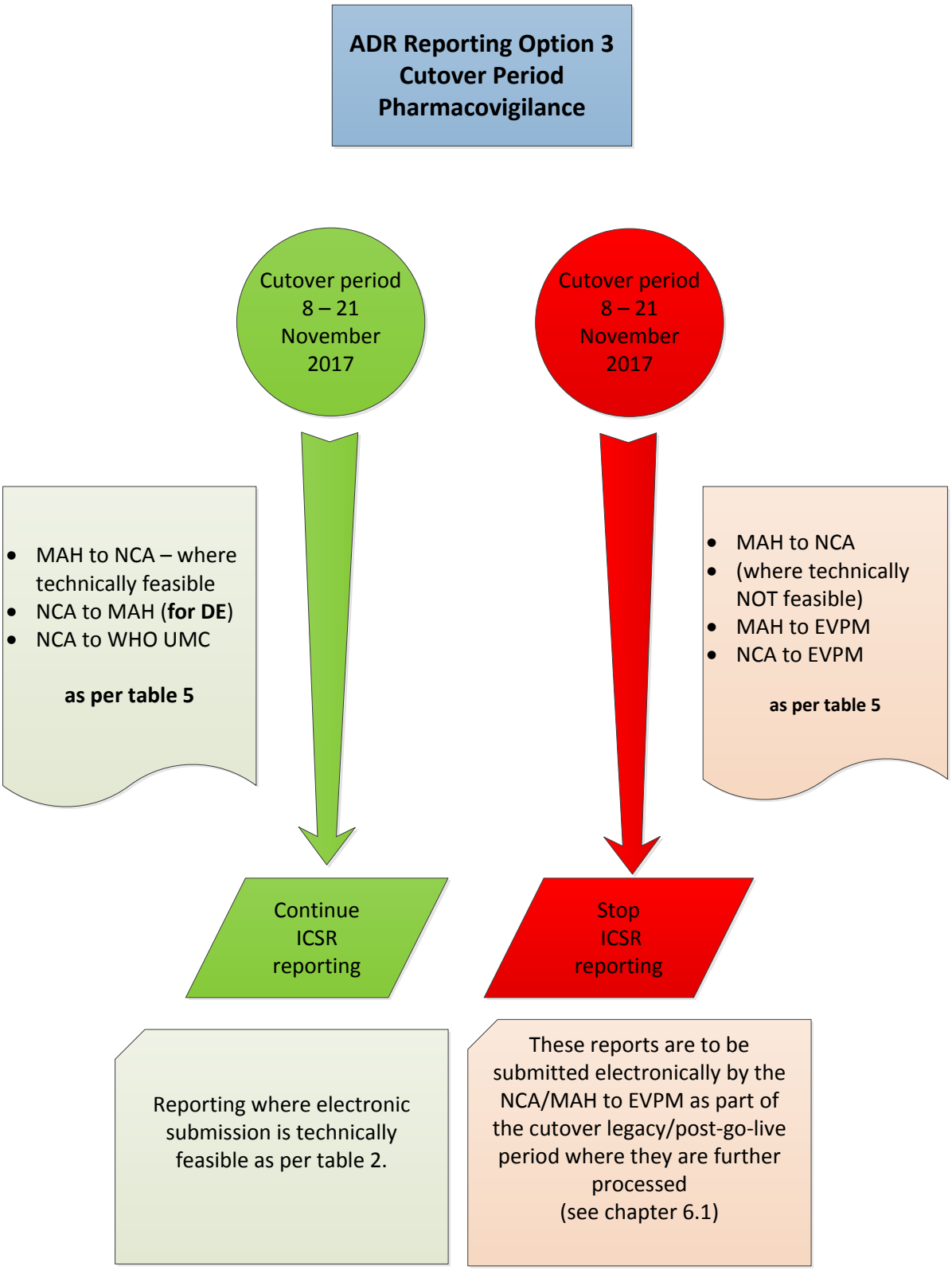


Figure 3: ADR reporting Option 3 during cutover period

Option 3 applies to the NCAs as reflected in table 5.

Table 5: NCAs for which ADR reporting according to option 3 during the cutover period applies

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
Medicines and Healthcare products Regulatory Agency	UK	3A	MHRA (HQ ORG-ID MHRAUK) will continue to receive from MAHs ICSRs during the cutover period. Where MAHs will not be able to report electronically (e.g. WEBTRADER companies) during the cutover period of 8 (0:00) to 21 (24:00), ICSRs have to be submitted electronically to EVPM by the MAH as part of the cutover legacy /post-go-live period **in accordance with the simplified reporting rules** as set out in the GVP Module VI (**Revision 2**) as of 22 November 2017 (see chapter 6.1). MHRA (HQ ORG-ID MHRAUK) will stop sending ICSRs to MAHs during the cutover period. MHRA will continue to send ICSRs to WHO-UMC. WHO UMC will need to review reports from MHRA/EVPM from the cutover period for potential duplicates (see figure 3b).
Bundesinstitut für Arzneimittel und Medizinprodukte	DE	3B	BfArM (HQ ORG-ID BFARM) will accept ICSRs electronically during the cutover period from 8-21 November 2017 and will continue to provide MAHs with ICSRs during this period. Due to its own transition process, the BfArM asks MAHs to stop ICSR-submission to the BfArM from 20 - 21 November 2017 considering the due date of those reports. With 22 November 2017, the centralised reporting will start and MAHs have to submit ICSRs to EudraVigilance. During EudraVigilance's cutover period, where MAHs will not be able to report electronically via EudraVigilance (e.g. WEBTRADER companies), MAHs may use an alternate way (common web portal for ADR submission by BfArM and PEI for EVWEB-users; dedicated mailbox for EVPOST-users). The exact details regarding the correct submission of ICSRs to the BfArM and PEI during the EudraVigilance

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
			cutover-period and national changes associated to the centralised reporting are published on BfArM's website (dedicated FAQ-document). BfArM will continue to provide WHO UMC with reports received until 21 (23:59) November 2017. **MAHs will need to exclude reports from BfArM from the cutover period when they start downloading ICSRs from the EudraVigilance ICSR download manager to avoid duplicates (see figure 3a).** WHO UMC will need to review reports from BfArM/EVPM from the cutover period for potential duplicates (see figure 3b).
Paul-Ehrlich Institute	DE	3B	PEI (HQ ORG-ID PEI) will accept ICSRs electronically during the cutover period from 8-21 November 2017 and will continue to provide MAHs with ICSRs during this period. PEI (HQ ORG-ID PEI) will continue to send ICSR messages electronically (E2B) to the DE-BfArM and German Society of Physicians (Arzneimittel Kommission der Deutschen Ärzteschaft - AkDÄ), which have been send to PEI via web-portal or hardcopy. During EV's cutover period, where MAHs will not be able to report electronically via EudraVigilance (e.g. WEBTRADER companies), MAHs may use an alternate way (common web portal for ADR submission by PEI and BfArM for EVWEB-users; dedicated mailbox for EVPOST-users). The exact details regarding the correct submission of ICSRs to the PEI and BfArM during the EV cutover-period and national changes associated to the centralised reporting are published on the website (dedicated FAQ-document). PEI will continue to provide WHO UMC with reports received until 21 (23:59) November 2017. **MAHs will need to exclude reports from PEI**

National Competent Authority / EudraVigilance (EVPM)	Member State	Option	Points to be taken into account
			from the cutover period when they start downloading ICSRs from the EudraVigilance ICSR download manager to avoid duplicates (see figure 3a). WHO UMC will need to review reports from PEI/EVPM from the cutover period for potential duplicates (see figure 3b).
EudraVigilance Post-Authorisation Module (EVPM)	EU	1	EVPM will stop receiving ICSRs from NCAs and MAHs as of 8 (00:00) November 2017.

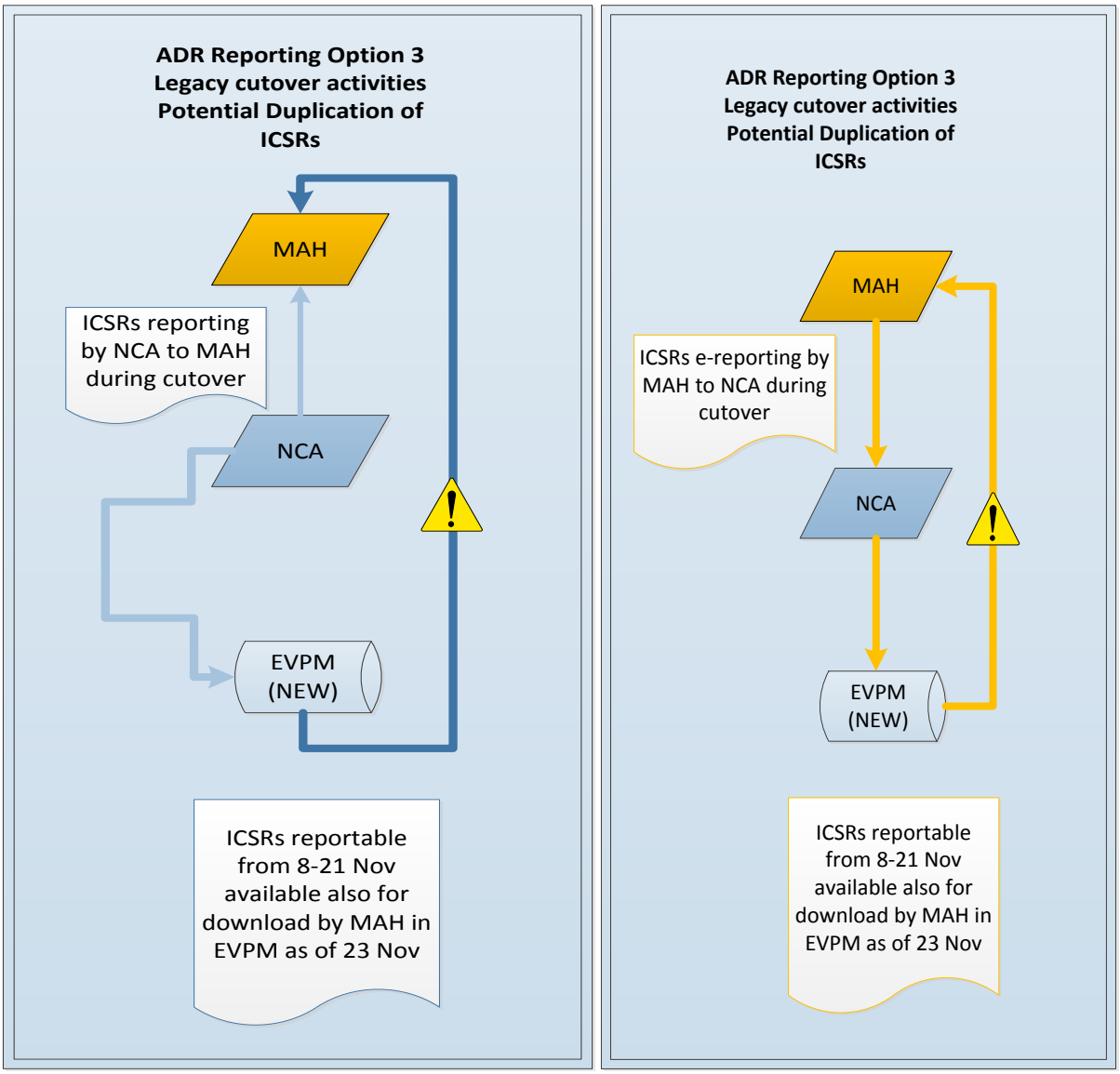


Figure 3a: MAH to manage potential duplicates from legacy cutover activities

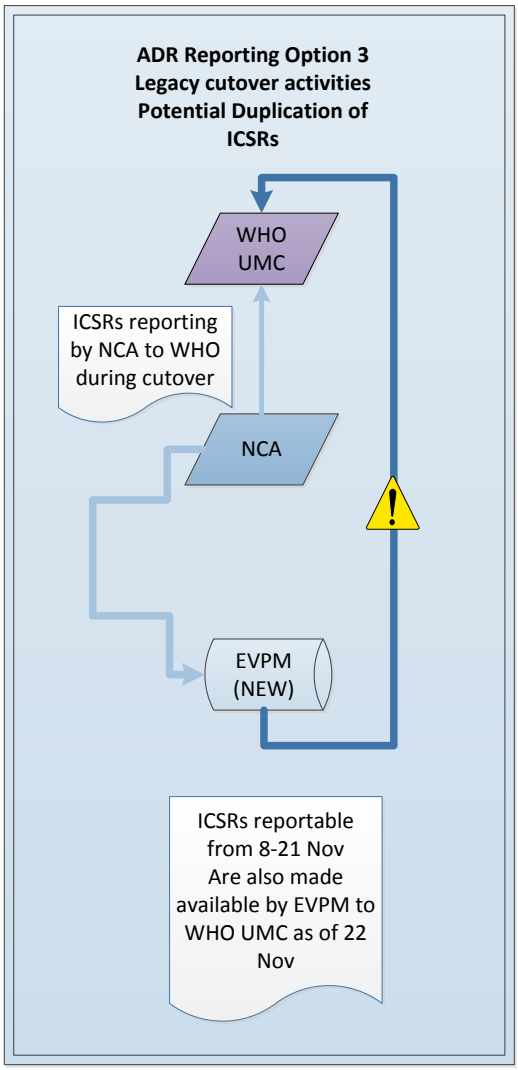


Figure 3b: MAH to manage potential duplicates from legacy cutover activities

5.2. *SUSAR reporting – clinical trials*

During the EudraVigilance cutover period, the reporting options as described in chapters 5.2.1 to 5.2.3 should be followed. The time indicated in the tables below refers to local time.

- Sponsors should notify Member States within 3 days of any action needed to protect the health and safety of clinical trial subjects.
- Sponsors should continue to report any safety issues not falling within the definition of SUSAR in accordance with the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01).
- With EVCTM not being available as of 8 November 2017, sponsors need to be aware that acknowledgement messages (ACKs) for safety messages sent on 6 and 7 November, may not be returned. This is due to the fact that ACKs may take up to 48 hours to be generated and returned by the receiver organisation by means of the EudraVigilance Gateway. Where no ACKS are received by the sender organisation (sponsor) for messages sent as of 6 November 2017, the message disposition notification (MDN) should serve as confirmation of the delivery of the message to the receiver organisation. **This is on the basis that the safety messages submitted were valid and did not contain errors.**

- **Safety messages must NOT be submitted to EVCTM during the cutover period!**
- **The safety messages will NOT be queued and will be discarded!**

5.2.1. SUSAR reporting - option 1 during cutover phase

During the cutover period, the sponsor of clinical trials stops the electronic submission of SUSARs from clinical trials.

This applies to the electronic submission of ICSRs from:

- A sponsor to a Member State;
- A sponsor to EVCTM**.**

No alternative arrangements for reporting by a sponsor of a clinical trial to a Member State apply during the cutover period.

As part of the cutover legacy period, these SUSAR reports are to be submitted electronically by the sponsor to the Member State as applicable and to EVCTM **(see chapter 6.2)** in accordance with the established reporting rules based on the principles of the Detailed guidance on the collection,

verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01).

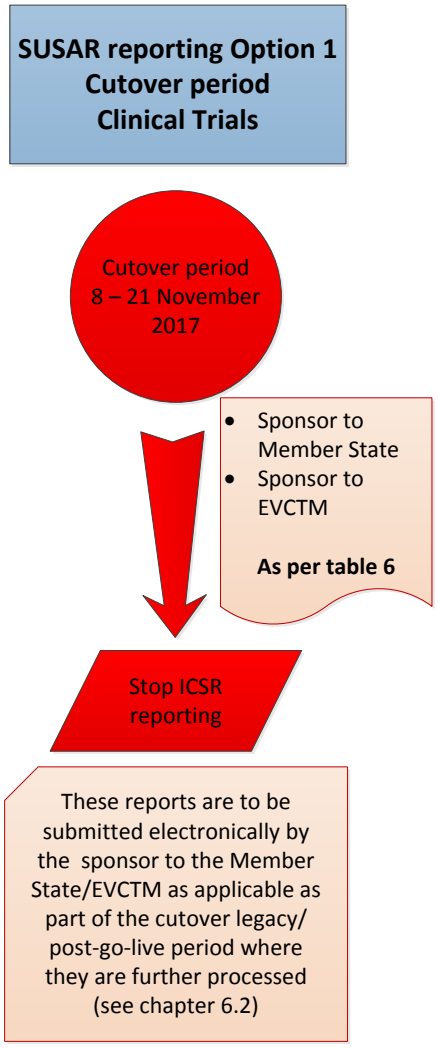


Figure 4: SUSAR reporting Option 1 during cutover period

Option 1 applies to Member States as reflected in table 6.

Table 6: Member States for which SUSAR reporting according to option 1 during the cutover period applies

National Competent Authority / EudraVigilance (EVCTM)	Member State	Option	Points to be taken into account
Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten - Agence Fédérale des Médicaments et des Produits de Santé	BE	1	The Belgian Agency (HQ ORG-ID AFIGP) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.

National Competent Authority / EudraVigilance (EVCTM)	Member State	Option	Points to be taken into account
Bulgarian Drug Agency – Ministry of Health	BG	1	The Bulgarian Agency (HQ ORG-ID BDA – Affiliate CTBDAP) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.
Ministry of Health – Pharmaceutical Services	CY	1	The Ministry of Health in Cyprus (HQ ORG-ID CYPPVPR) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.
Ravimiamet	EE	1	The Estonian Agency (HQ ORG-ID SAM) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.
Lääkealan turvallisuus- ja kehittämiskeskus	FI	1	The Finish Agency (HQ ORG-ID FINAM, affiliate FINAMW) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.
Health Products Regulatory Authority/An tÚdarás Rialála Táirgí Sláinte	IE	1	The Irish Agency **HPRA (HQ ORG-ID IMB affiliate IMBCT) will stop receiving ICSRs from sponsors from 4 (00:00) to 21 November (24:00) 2017.** Any SUSARs sent to EVCTM from 4 to 7 November should be submitted to HPRA after 22 November along with the other cutover legacy SUSARs. In accordance with the national Guide to Clinical Trials Applications, sponsors and investigators are obliged to notify the HPRA within 3 days of any action needed to protect the health and safety of clinical trial subjects.
Office of Health / Medicinal Products Control Agency	LI	1	The Liechtenstein Agency (HQ ORG-ID KARZNEI) will stop receiving ICSRs from sponsors as of 8 (00:00) November 2017. As of 22 November 2017 all ICSRs should be submitted to EVCTM.

National Competent Authority / EudraVigilance (EVCTM)	Member State	Option	Points to be taken into account
Valstybinė vaistų kontrolės tarnyba prie Lietuvos Respublikos sveikatos apsaugos ministerijos	LT	1	The Lithuanian Agency (HQ ORG-ID SMCAP, affiliate SMACACTP) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.
Zāļu valsts aģentūra	LV	1	The Latvian Agency (HQ ORG-ID LRZBP2005, affiliate LRKPN2005) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.
Awtorità dwar il-Mediċini	MT	1	The Maltese Agency (HQ ORG-ID ADM) will stop receiving ICSRs from sponsors as of 8 (00:00) November 2017.
Central Committee on Research Involving Human Subjects (CCMO) or Ministry of Health	NL	1	The Dutch authorities will stop receiving SUSARs from sponsors from 8 (00:00) to 21 (24:00) November 2017. Sponsors shall continue with the SUSAR reporting to the Dutch Medical Review Ethics Committees as per the currently established process. This will not be impacted by the cutover period.
Statens legemiddelverk	NO	1	The Norwegian Agency (HQ ORG-ID NOMACT) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.
Läkemedelsverket	SE	1	The Swedish Agency (HQ ORG-ID SEMPA) should not receive any SUSARs from sponsors during the cutover period, according to the current practice.
EudraVigilance Clinical Trial Module (EVCTM)	EU	1	EVPM will stop receiving ICSRs from NCAs and MAHs from 8 (00:00) to 21 (24:00) November 2017.

5.2.2. SUSAR reporting - option 2 during cutover phase

During the cutover period, the sponsor of clinical trials stops the electronic submission of SUSARs (figure 5)**.**

This applies for the electronic submission of ICSRs from:

- A sponsor to a Member State;
- A sponsor to EVCTM.

The sponsor has to follow alternative arrangements for reporting to the Member State during the cutover period based on one of the following provisions:

A. The sponsor sends **all SUSAR report(s)** in an internationally acknowledged format (CIOMS I) to a dedicated fax line (in paper format), to a dedicated e-mail (in pdf format) or via post (in paper format) to the Member State and writes "**SUSAR reporting - Failure of safety message generation at receiver's side**" on the paper report(s)/email/letter. **The email subject/fax cover sheet should specify "SUSAR reporting cutover period".**

B. The sponsor sends **all fatal/life threatening SUSAR report(s)** in an internationally acknowledged format (CIOMS I) to a dedicated fax line (in paper format), to a dedicated e-mail (in pdf format) or via post (in paper format) to the Member State and writes "**SUSAR reporting - Failure of safety message generation at receiver's side**" on the paper report(s)/email/letter.

In addition, two cumulative line listings of all SUSARs should be provided for fatal/life threatening and non-fatal/non-life-threatening SUSARS for the following reference period:

- Line listing 1: covering period 8-13 November and to be submitted on 14 November 2017
- Line listing 2: covering period 14 -20 November to be submitted on 21 November 2017

The line listings should be based on IMPs (investigational medicinal products) and should include the reference to the IMP and EudraCT number (to allow Member States to monitor the IMPs over all studies). For each of the line listings, individual cases in CIOMS I format should be also provided. **The email subject/fax cover sheet should specify "SUSAR reporting cutover period" for CIOMS reports .The email subject/fax cover sheet should specify "SUSAR", "Line listing 1- IMP/EudraCT number" or "Line listing 2- IMP/EudraCT number" cutover period.**

SUSAR reporting for the alternative arrangements has to follow the established reporting rules based on the principles of the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01).

As part of the cutover legacy period (see chapter 6.2), these SUSAR reports are to be submitted electronically by the sponsor to the Member State as applicable and to EVCTM in accordance with the established reporting rules based on the principles of the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01).

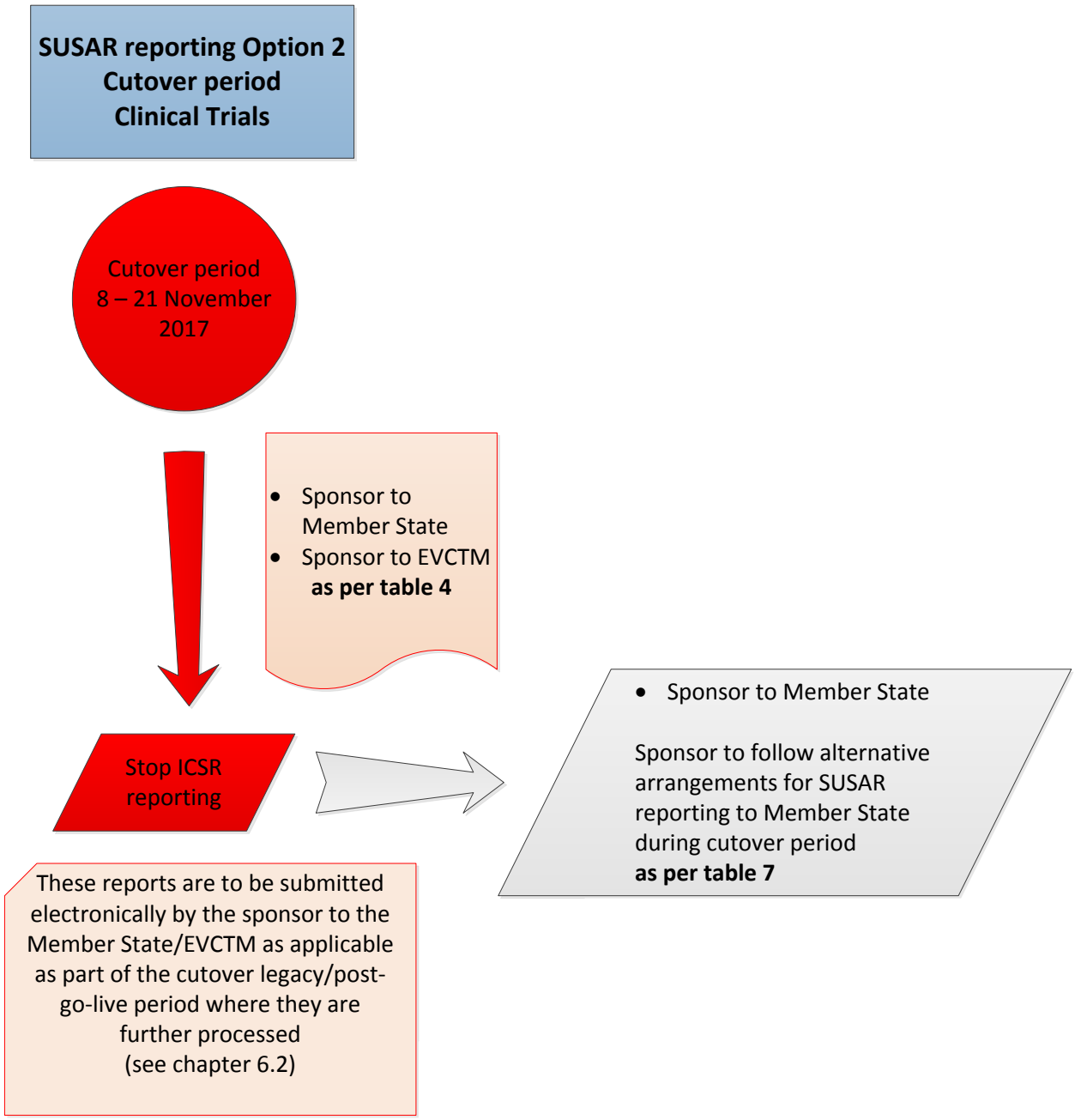


Figure 5: SUSAR reporting Option 2 during cutover period

Option 2 applies to Member States as reflected in table 7.

Table 7: Member States for which SUSAR reporting according to option 2 during the cutover period applies

National Competent Authority EudraVigilance (EVCTM)	Member State	Option	Alternative arrangements
BASG - Bundesamt für Sicherheit im Gesundheitswesen	AT	2B	The Austrian Agency (HQ ORG-ID BDA, affiliate BASGAGESCT) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports should be transmitted in CIOMS I format to: Email: pharm-vigilanz@ages.at or Fax: +43 (0) 50 555 36207 or Post: BASG - Bundesamt für Sicherheit im Gesundheitswesen AGES - Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH Traisengasse 5 A-1200 Wien Austria Emails will be registered and acknowledged.
Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet	HU	2A	The Hungarian Agency (Affiliate OGYI) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports should be transmitted in CIOMS I format to: Email: clinadr@ogyei.gov.hu Emails will be registered and acknowledged. When the new EudraVigilance system goes live, the sender organisations (sponsor) should transmit electronically all emailed

National Competent Authority EudraVigilance (EVCTM)	Member State	Option	Alternative arrangements
			report(s) as ICSRs as usual.
Státní ústav pro kontrolu léčiv	CZ	2A	The Czech Agency (HQ ORG-ID CZSUKL, affiliate CZSUKLCT) will stop receiving ICSRs from sponsors from 7 (00:00) to 21 (24:00) November 2017. SUSAR reports should be transmitted in CIOMS I format by email to: klinsekret@sukl.cz (pdf format). As of 22 Nov SUSARs are to be submitted by sponsors to EVCTM only.
Danish Medicines Agency	DK	2B	The Danish Agency DKMA (HQ ORG-ID DKMAEUDRA, affiliate DKMACTM) will stop receiving ICSRs from sponsors from 6 (12:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format and line listings should be transmitted to: FAX: +45 44889599 Danish legislation concerning sensitive personal information does not allow transmission via un-encrypted e-mail. Any SUSARs from 6 (12:00) and 7 November should be submitted by MAHs to EVCTM after 22 November along with the other cutover legacy ICSRs.
Agencia Española de Medicamentos y Productos Sanitarios	ES	2B	The Spanish Agency (HQ ORG-ID AGEMEDCT) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format and line listings should be

National Competent Authority EudraVigilance (EVCTM)	Member State	Option	Alternative arrangements
			transmitted to: FAX:+34 918 225 076
National Organization for Medicines	GR	2B	The Greek Agency (HQ ORG-ID GREOF) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format and line listings should be transmitted by: Email: ev@eof.gr (pdf format) or Fax: +30 210 6549585
Agenzia Italiana del Farmaco	IT	2B	The Italian Agency AIFA (HQ ORG-ID MINISAL02, affiliate AIFACT) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format and line listings should be transmitted by: Email: SUSAR_ITA@aifa.mailcert.it
Agencija za Lijekove i Medicinske Proizvode	HR	2A	The Croatian Agency (HQ ORG-ID ALMP) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports should be transmitted in CIOMS I format by email to: ispitivanja@halmed.hr
Urząd Rejestracji Produktów Leczniczych, Wyrobow Medycznych i Produktów Biobójczych	PL	2A	The Polish Agency (HQ ORG-ID URPL) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format should be transmitted by: Fax: +48 22 49-21-299 or Fax: +48 22 49-21-109 or

National Competent Authority EudraVigilance (EVCTM)	Member State	Option	Alternative arrangements
			Email: pl_cebk@urpl.gov.pl (pdf format) or Post: Department of Clinical Trial of Medicinal Products, The Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Al. Jerozolimskie 181 C, 02-222 Warsaw, Poland
INFARMED - Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.	PT	2B	The Portuguese Agency (HQ ORG-ID INFARMED) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format and line listings should be transmitted by: Email: ensaios.clinicos@infarmed.pt or Fax: +351 217987248
Agentia Națională a Medicamentului şi a Dispozitivelor Medicale	RO	2A	The Romanian Agency (HQ ORG-ID NMA) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format should be transmitted by: Email: farmacovigilenta@anm.ro
Javna agencija Republike Slovenije za zdravila in medicinske pripomočke	SI	2B	The Slovenian Agency (HQ ORG-ID ARSZMP) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format and line listings should be transmitted by: Email: CT@jazmp.si

National Competent Authority EudraVigilance (EVCTM)	Member State	Option	Alternative arrangements
Štátny ústav pre kontrolu liečiv	SK	2B	The Slovakian Agency (HQ ORG-ID SUKLSK) will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017. SUSAR reports in CIOMS I format and line listings should be transmitted by: Email: trial-sukl@sukl.sk
EudraVigilance Clinical Trial Module (EVCTM)	EU	1	EVPM will stop receiving ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.

5.2.3. SUSAR reporting - option 3 during cutover phase

During the cutover period (figure 6)**:**

- the sponsor of clinical trials continues with the electronic submission of ICSRs to the Member State **where this is technically feasible** in accordance with table 2; or
- the sponsor of clinical trials continues with the current established reporting method for SUSARs to the Member State.

Where electronic reporting is NOT feasible, the sponsor has to follow alternative arrangements for reporting to the Member State during the cutover period based on one of the following provisions:

A. The sponsor sends **all SUSAR report(s)** in an internationally acknowledged format (CIOMS I) to a dedicated fax line (in paper format), to a dedicated e-mail (in pdf format) or via post (in paper format) to the Member State.

B. The sponsor sends **all fatal/life threatening SUSAR report(s)** in an internationally acknowledged format (CIOMS I) to a dedicated fax line (in paper format), to a dedicated e-mail (in pdf format) or via post (in paper format) to the Member State and writes "**SUSAR reporting - Failure of safety message generation at receiver's side**" on the paper report(s)/email/letter.
In addition, two cumulative line listings of all SUSARs should be provided for fatal/life threatening and non-fatal/non-life-threatening SUSARS for the following reference period:

- Line listing 1: covering period 8-13 November and to be submitted on 14 November 2017
- Line listing 2: covering period 14 -20 November to be submitted on 21 November 2017

The line listings should be based on IMPs (investigational medicinal products) and should include the reference to the IMP and EudraCT number (to allow Member States to monitor the IMPs over all studies). For each of the line listings, individual cases in CIOMS I format should

be also provided. **The email subject/fax cover sheet should specify "SUSAR". The email subject/fax cover sheet should specify "SUSAR", "Line listing 1- IMP/EudraCT number" or "Line listing 2- IMP/EudraCT number".**

C. The sponsor submits SUSARs based on established national reporting procedures.

The reporting for the alternative arrangements has to follow the established reporting rules based on the principles of the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01).

As part of the cutover legacy period (see chapter 6.2), these reports are to be submitted electronically by the sponsor to the Member State as applicable and to EVCTM in accordance with the established reporting rules based on the principles of the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01).

During the cutover period, the electronic submission of SUSARs **by a sponsor to EVCTM** is to be **STOPPED**.

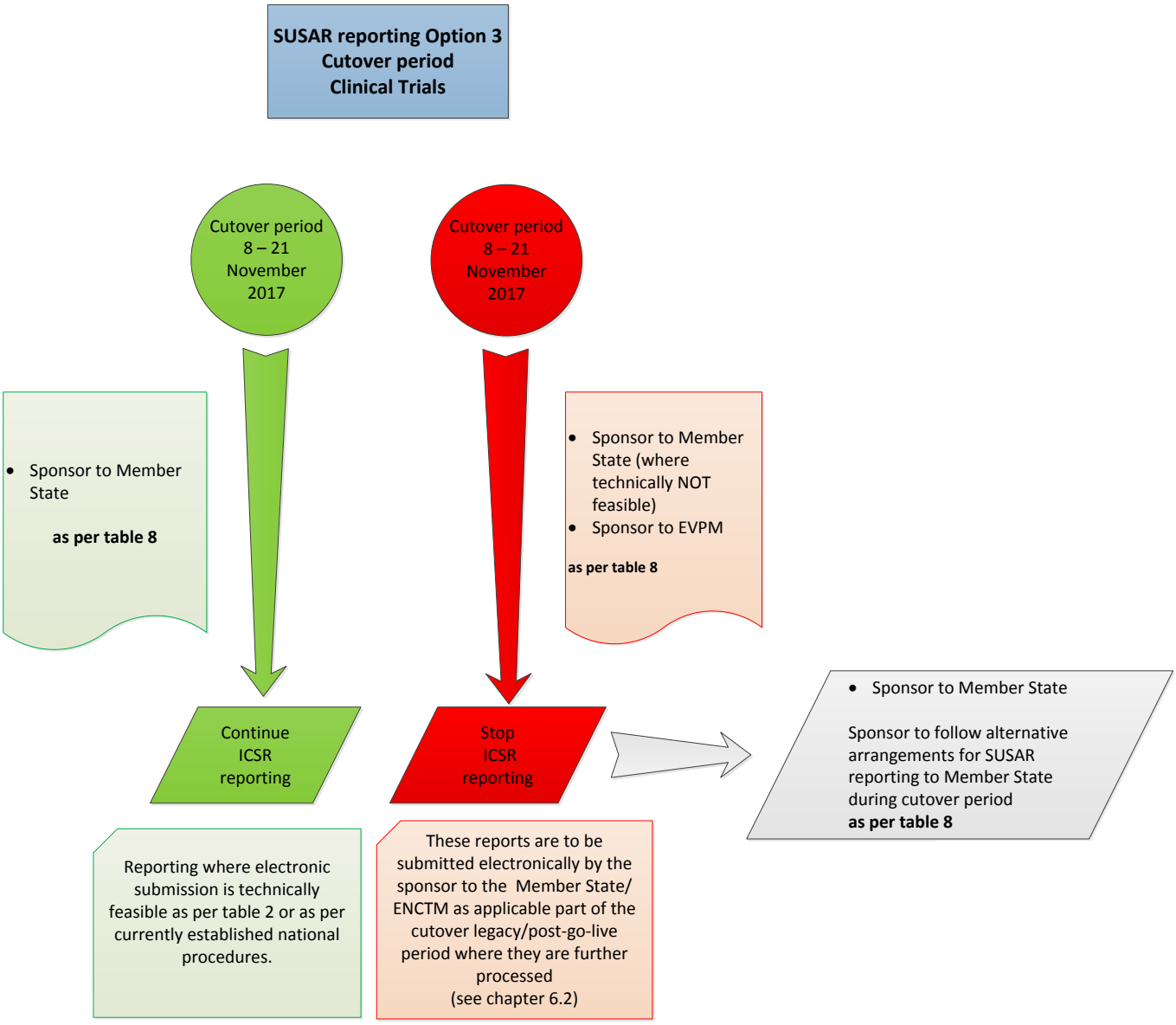


Figure 6: SUSAR reporting Option 3 during cutover period

Option 3 applies to the Member States specified in table 8.

Table 8: Member States for which SUSAR reporting according to option 3 during the cutover period applies

National Competent Authority	Member State	Option	Alternative Arrangements
Bundesinstitut für Arzneimittel und Medizinprodukte	DE	3C	BfArM will continue to receive SUSARs electronically in ICSR format during the cutover period from 8-21 November 2017 based on the currently established process. The exact details regarding the correct submission of ICSRs to the BfArM and PEI during the EV cutover-period and national changes associated to the centralised reporting are published on BfArM's website (dedicated FAQ-document).
Paul-Ehrlich Institute	DE	3C	DE-PEI will continue to receive SUSARs electronically in ICSR format during the cutover period from 8-21 November 2017 based on currently established process. The exact details regarding the correct submission of ICSRs to the PEI and BfArM during the EV cutover-period and national changes associated to the centralised reporting are published on the website.
Agence nationale de sécurité du médicament et des produits de santé	FR	3C	The French Agency ANSM (HQ ORG-ID AFSSAPS) will continue to receive SUSARs by email with CIOMS pdf files attached as per currently established process.
Ministère de la Santé	LU	3C	The Luxemburg Agency (HQ ORG-ID DPM) will continue to receive SUSARs by email with CIOMS pdf files attached as per currently established process. E-mail address: clinicaltrials@ms.etat.lu
Lyfjastofnun	IS	3C	The Islandic Agency (HQ ORG-ID ADALIMCA01) will stop receiving ICSRs from sponsors as of 8 (00:00) November 2017. Sponsors should report using the IMA web-portal.
Medicines & Healthcare products Regulatory Agency (MHRA)	UK	3B	MHRA (HQ ORG-ID MHRAUK, affiliate MHRACTU) will continue to receive ICSRs from sponsors from 8 (00:00) to 21 (24:00) November 2017.

5.3. *Medical literature monitoring (MLM) by the Agency*

During the EudraVigilance cutover period, the MLM service ***will continue*** to search for and screen medical literature articles. The MLM service will also continue to prepare the corresponding tracking sheets for all active substances in scope of the MLM service.

- During the cutover period, the MLM tracking sheets which contain the search and screening results will not be published at the restricted area of EudraVigilance.
- No ICSRs will be generated related to valid cases identified as part of the MLM service and MLM cases cannot be accessed via EVWEB or downloaded by means of the MLM Export Manager.

5.4. *Data submission on medicines to the XEVMPD*

- During the EudraVigilance cutover period the data submission on medicines (Article 57) by MAHs using the XEVMPD and keeping this information up-to-date in accordance with Article 57 of Regulation (EC) No 726/2004 will not be possible.

- **XEVPRM messages must NOT be submitted to the XEVMPD during the cutover period!**
- **The product messages will not be queued and will be discarded!**

5.5. *Signal Management by NCAs and EMA*

During the EudraVigilance cutover period, EVDAS will be available for NCAs and EMA based on a data set up to the 7 November 2017:

- NCAs and EMA will continue the **signal management** in the EEA in accordance with (GVP) Module IX – Signal management, as per normal process by NCAs and EMAs using eRMRs and/or EVDAS with data lock point of 7 November 2017.

- The last eRMR for EMA and NCAs in the EEA before the cutover period will be provided to NCAs on 8 November 2017. The routine eRMR (monthly) will cover the reference period 2 October to 5 November 2017. *Note: the hyperlinks in the eRMRs produced until 8 November will be working*

until 21 November 2017.

- The routine eRMR (six months) will cover the reference period 8 May to 5 November and will be provided to NCAs on 22 November with the hyperlinks working for the new EVDAS.
- The additional eRMR scheduled for the 15 November covering the reference period 23 October to 12 November 2017 will not be produced.

5.6. *Adrreports.eu portal*

During the EudraVigilance cutover period, the public will be able to access information on suspected adverse reactions related to medicines at the adrreports.eu portal. The EudraVigilance data set will be based on the cut-off date of 31 October 2017.

5.7. *Interoperability testing with the new EudraVigilance XCOMP (test) environment*

Organisations can continue to perform interoperability testing. For details refer to chapter 4.4.

6. EudraVigilance cutover legacy activities

Following the EudraVigilance cutover period and the launch of the new EudraVigilance system on 22 November 2017, **there will be legacy activities as a consequence of the cutover period** that will need to be initiated on 22 November 2017 **with the aim of completion by 24 November 2017**.

This refers to the areas described in this chapter.

ID	Task Name	Start	Finish	Duration
1	EudraVigilance cutover legacy	22/11/2017	24/11/2017	3d
2	EudraVigilance go-live	22/11/2017	22/11/2017	0d
3	ADR reporting: ICSRs that could not be submitted during cutover: simplified rules	22/11/2017	24/11/2017	3d
4	SUSAR reporting: ICSRs that could not be submitted by sponsors during cutover	22/11/2017	24/11/2017	3d
5	Medical literature monitoring by EMA	22/11/2017	30/11/2017	7d
6	Data submission on medicines (Art 57)	22/11/2017	30/11/2017	7d
7	Signal management by EMA and NCAs	22/11/2017	06/12/2017	11d
8	EudraVigilance registration of organisations and users	22/11/2017	29/12/2017	28d
9	Adrreports.eu portal – data aggregation/ publication	22/11/2017	22/11/2017	0d
10	EV XCOMP interoperability testing by stakeholders	22/11/2017	29/12/2017	28d

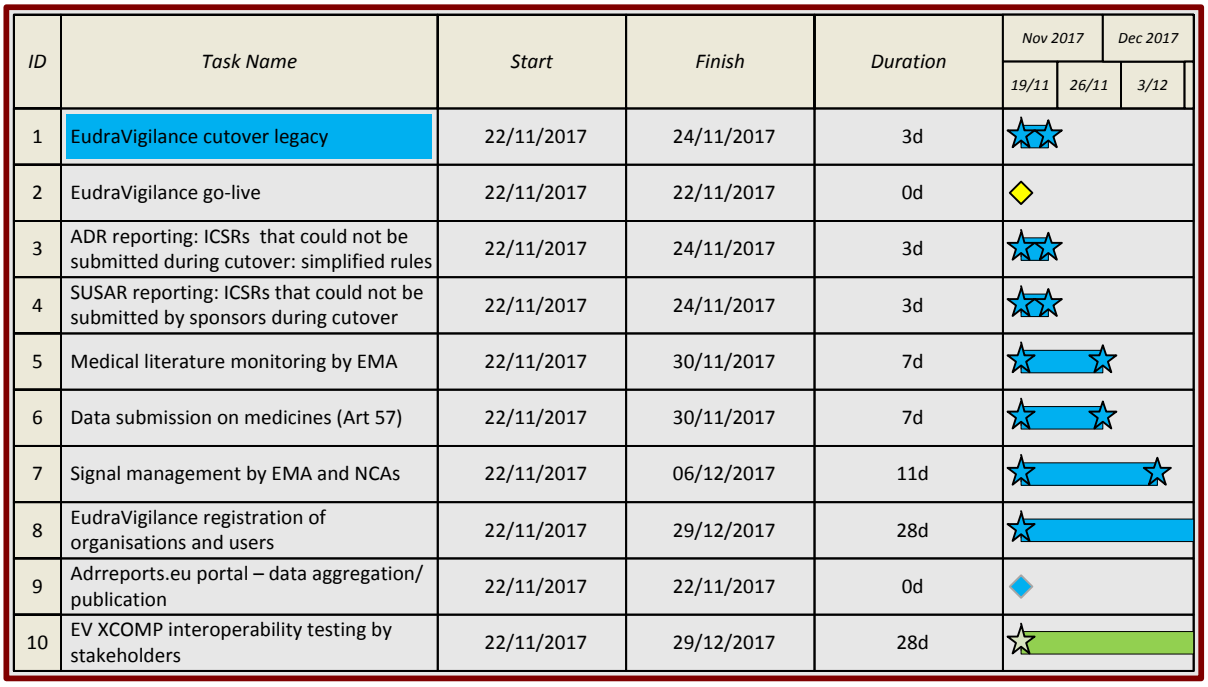


Chart 3: Business processes as a result of the cutover phase (Note: duration is indicated in business days excluding weekends)

6.1. *ADR reporting (pharmacovigilance) - legacy activities from cutover period*

For ICSRs that could not be submitted electronically during the cutover period as described in chapter 5.1, the following principles apply (figure 7):

- **MAHs need to submit electronically to EVPM** information on all **serious suspected adverse reactions** that occurred in the EEA and in third countries. This refers to reports of which the MAH gained knowledge *before the 22 November 2017 and which could not be submitted electronically before or during the cutover period.* The submission of ICSRs requiring reporting from 8 to 21 November (according to 15 days reporting timelines) should take place within 2 EMA business days following the go-live of EudraVigilance. EudraVigilance will reroute the reports to the applicable NCAs based on the rerouting rules defined by the NCAs. The reporting follows the simplified reporting rules as set out in **GVP Module VI (revision 2)**.
- **MAHs need to submit electronically to EVPM** information on all **non-serious suspected adverse reactions** that were reportable to NCAs in the EEA. This refers to reports of which the MAH gained knowledge *before the 22 November 2017 and which could not be submitted electronically the NCA before or during the cutover period in accordance with table 3 of the document "*Reporting requirements of Individual Case Safety Reports (ICSRs) applicable to marketing authorisation holders during the interim period" (EMA/411742/2015 Rev. 9). The submission of non-serious ICSRs requiring reporting according to table 3 between 8 to 21 November should take place within 2 EMA business days following the go-live of EudraVigilance. EudraVigilance will reroute the reports to the applicable NCAs if they choose to receive them. The reporting follows the simplified reporting rules as set out in **GVP Module VI** (**revision 2**).
- **MAHs need to use EVWEB functionalities to obtain access** (and to download) reports of suspected adverse reactions from NCAs in the EEA. This refers to reports of which the NCAs gained knowledge *before the 22 November 2017 and which were not submitted electronically/provided by the NCA before or during the cutover period.*
- **NCAs in the EEA** need to **submit reports of suspected adverse reactions** that were reportable **to EVPM** electronically to EudraVigilance. This refers to reports of which the NCA gained knowledge *before the 22 November 2017 and which could not be submitted electronically by a NCA before or during the cutover period.* The submission of ICSRs requiring reporting between 8 to 21 November should take place within 2 EMA business days following the go-live of EudraVigilance. The reporting follows the simplified reporting rules as set out in GVP Module VI (**revision 2**).
- **Reports of suspected adverse reactions** with an occurrence country in the EEA and reported by NCAs and MAHs following the cutover period to EVPM, **will be made available to WHO UMC within the agreed timelines**.

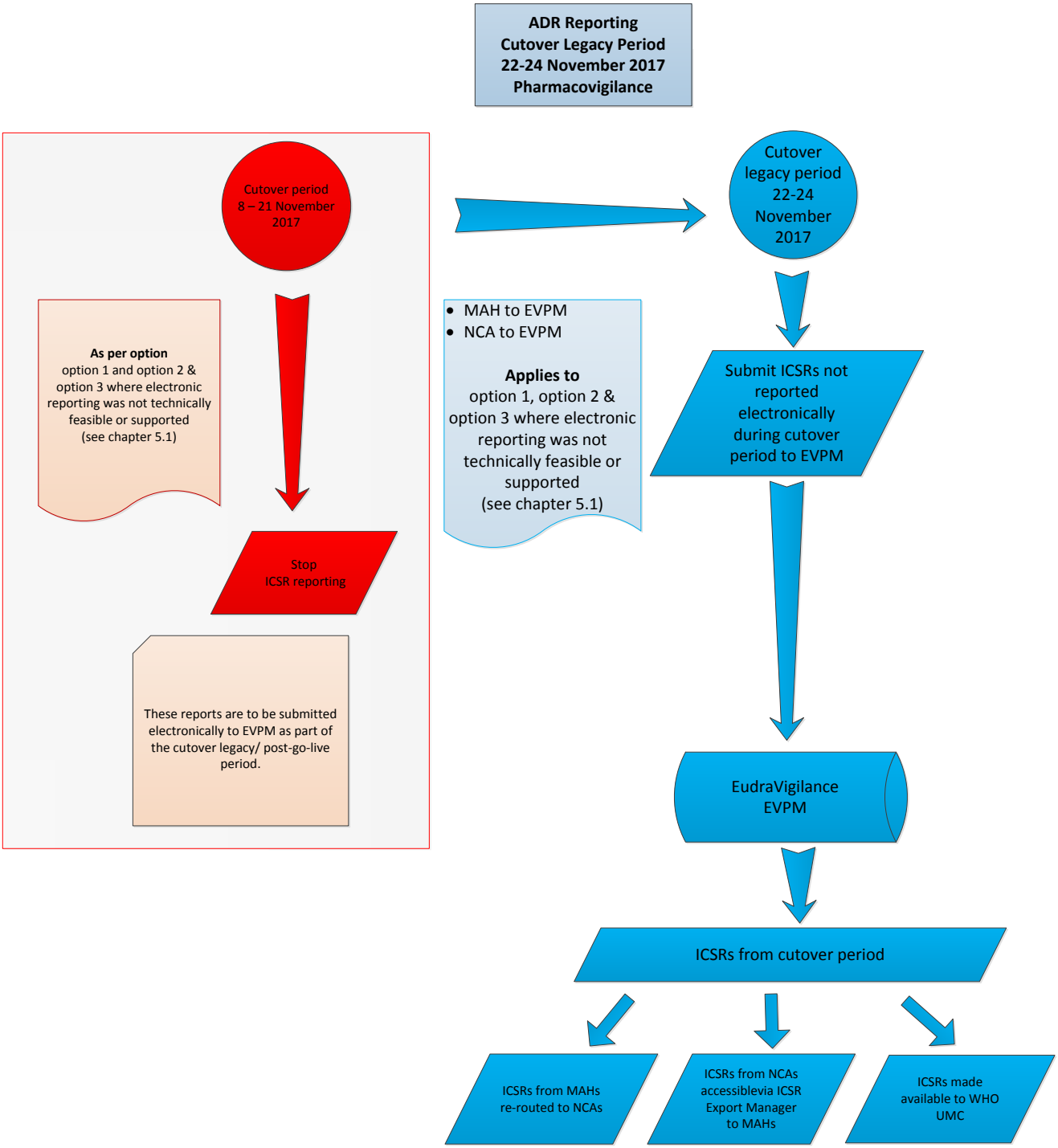


Figure 7: Electronic ADR reporting for cutover legacy period

- Reports that are submitted within 2 EMA business days of the gateway and the new EudraVigilance system being made available after the downtime will have the reporting compliance calculated against the first day of new EudraVigilance system downtime i.e. 8 November 2017.
- For compliance monitoring in EudraVigilance, the downtime will include the two business days during which the “legacy reports” are to be submitted to EudraVigilance.

- MAHs and NCAs should put mechanisms in place to validate that all reportable suspected adverse reactions are electronically submitted to EVPM, after the cutover period is finalised.
- Error reports need to be corrected and ICSRs resubmitted.
- MAHs and NCAs need to comply with the security principles and responsibilities applicable to the use of EudraVigilance.

6.2. *SUSAR reporting from clinical trials - legacy from cutover period*

For SUSAR reports that could not be submitted electronically prior to the initiation of the cutover period, the following principles apply (figure 8):

- Sponsors need to submit SUSARs related to clinical trials electronically according to the present arrangements and reporting requirements as set out in Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use (‘CT-3’)(2011/C 172/01) (see chapter 7.4. SUSARs reported to the national competent authority (directly or indirectly through EVCTM)).
- This refers to reports of which the sponsor gained knowledge *and which could not be submitted electronically before or during the cutover period.* The electronic submission of SUSARs requiring reporting between 8 to 21 November (according to 7/15 days reporting timelines) should take place within 2 EMA business days following the go-live of EudraVigilance.

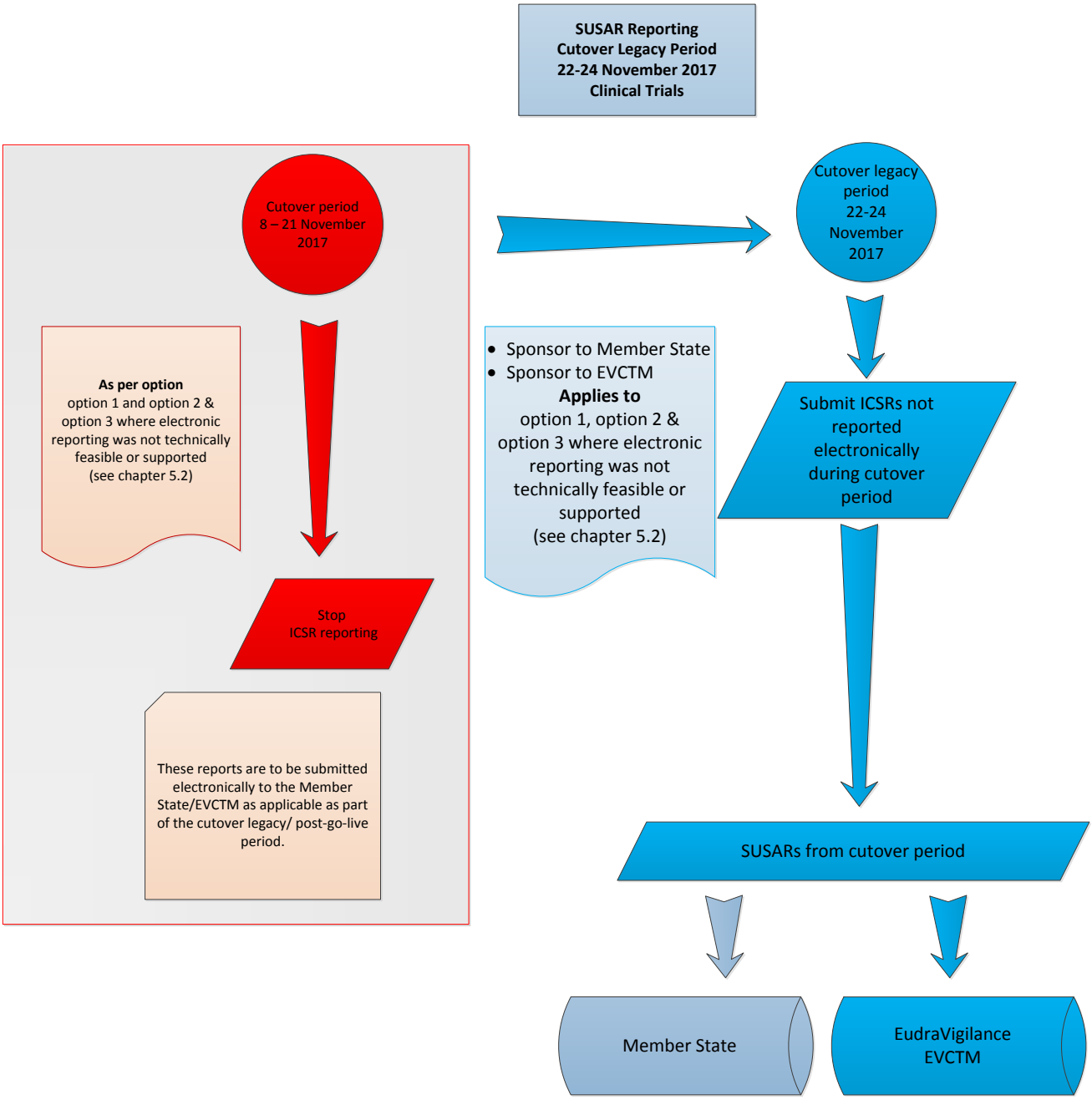


Figure 8: Electronic SUSAR reporting for cutover legacy period

- Reports that are submitted within 2 EMA business days of the gateway and the new EV system being made available after the downtime will have the reporting compliance calculated against the first day of new EudraVigilance system downtime i.e. 8 November 2017.
- For the compliance monitoring the downtime will include the two business days during which the legacy reports are to be submitted to EudraVigilance.

- Sponsors and NCAs should put mechanisms in place to validate that all reportable SUSARs are electronically submitted to EVCTM, after the cutover period is finalised.
- Error reports need to be corrected and resubmitted.
- Sponsors and NCAs need to comply with the security principles and responsibilities applicable to the use of EudraVigilance.

6.3. *Medical literature monitoring (MLM) by the Agency*

For ICSRs resulting from the MLM service that could not be processed or submitted electronically prior to the initiation of the cutover period, the following principles apply:

- The MLM tracking sheets with the search and screening results *will be published* at the restricted area of EudraVigilance on 22 November 2017. This refers to the tracking sheets that cover the MLM search and screening activities during the cutover period.
- *V*alid cases related to the MLM tracking sheet covering the cutover period will be entered into EVPM from 20 to 30 November 2017 and the ICSR tracking sheet published daily as of 22 November 2017.
- MAHs can download MLM cases using the EVWEB ICSR download **manager as of 23 November 2017**.

6.4. *Data submission on medicines to the XEVMPD*

For XEVPRMs that could not be submitted to XEVMPD prior to the initiation of the cutover period, the following principles apply:

- MAHs should reinitiate the data submission on medicines (Article 57) for new medicinal products or updates to existing medicinal products as of 22 November 2017.

- For the data submission on medicines, EudraVigilance version 7.0 should be continued to be used. The URL is as follows: https://eudravigilance.ema.europa.eu/X/

6.5. *Signal management*

- The ETL will run daily to refresh the data in EVDAS based on the legacy data submitted following the end of the cutover period.
- EMA and NCAs in the EEA can perform signal management in accordance with (GVP) Module IX – Signal management.

- The routine eRMR (six month) (reference period 8 May to 5 November) will be provided on 22nd November to have the hyperlinks working for the new EVDAS.
- The additional eRMR scheduled for the 15 November (reference period 23rd October to 12 November 2017) will not be produced.

6.6. *EudraVigilance registration of organisation / users*

The registration process of new organisations and users continues in accordance with the process and the phased EVDAS registration schedule as described at the EudraVigilance: how to register webpage.

6.7. *Interoperability testing with the new EudraVigilance XCOMP (test) environment*

Organisations can continue to perform interoperability testing. For details refer to chapter 4.4.

6.8. *Adrreports.eu portal*

The adrreports.eu portal will be launched with the new functionalities and the data set refreshed as of 7th November 2017.

7. EudraVigilance go-live production phase

With the go-live of the new EudraVigilance system, the simplified reporting rules as well as the new signal management process by MAHs will become applicable in pharmacovigilance (see **GVP Module VI (revision 2) and GVP Module IX (revision 1)**.

The reporting rules for SUSARs from clinical trials set out in Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')(2011/C 172/01) and established reporting procedures remain unchanged.

- The new EudraVigilance system launched on 22 November refers to version 8.0.

  The URL for the new production environment is as follows:

  https://eudravigilance-human.ema.europa.eu/#/

7.1. *Go-live timing*

All the new enhanced functionalities of the EudraVigilance system will be activated on the 22nd November 2017 at 09:00 UK time.

ID	Task Name	Start	Finish	Duration
1	**EudraVigilance post-go-live production**	22/11/2017	29/12/2017	28d
2	EudraVigilance go-live	22/11/2017	22/11/2017	0d
3	ADR reporting – simplified rules	22/11/2017	29/12/2017	28d
4	SUSAR reporting for clinical trials by sponsors	22/11/2017	29/12/2017	28d
5	Medical literature monitoring by EMA	22/11/2017	29/12/2017	28d
6	Data submission on medicines (Art 57)	22/11/2017	29/12/2017	28d
7	Signal management by EMA and NCAs	22/11/2017	29/12/2017	28d
8	Signal management by MAHs	22/11/2017	29/12/2017	28d
9	EudraVigilance registration of organisations and users	22/11/2017	29/12/2017	28d
10	Adrreports.eu portal – data aggregation/ publication	22/11/2017	29/12/2017	28d
11	EV XCOMP interoperability testing by stakeholders	22/11/2017	29/12/2017	28d

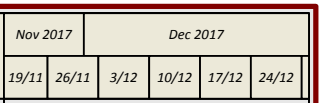


Chart 3: Business processes go-live production phase (Note: duration is indicated in business days excluding weekends)

7.2. *ADR reporting (pharmacovigilance) – simplified reporting rules*

NCAs, MAHs and EMA need to comply with the provisions set out in the Guideline on good pharmacovigilance practices: Module VI – Management and reporting of adverse reactions to medicinal products **(revision 2)**.

For the reporting of suspected adverse reactions related to medicines the following applies (see figure 9):

- **MAHs need to submit electronically** to EVPM information on **all serious suspected adverse reactions that occur in the Union and in third countries within 15 days** following the day on which the MAH concerned gained knowledge of the event.
  MAHs should stop sending ICSRs to the national competent authorities (NCAs) as of 22 November 2017 (see chapter 3.1 option 3) or earlier as specified in options 1 and 2 described in chapter 3.1.
- **MAHs need to submit electronically** to EVPM information on **all non-serious suspected adverse reactions that occur in the Union**, **within 90 days** following the day on which the MAH concerned gained knowledge of the event.

  MAHs should stop sending ICSRs (non-serious) to the national competent authorities (NCAs) as of 22 November 2017 (see chapter 3.1 option 3) or earlier as specified in options 1 and 2 described in chapter 3.1. This applies to NCAs, which required reporting of non-serious adverse reactions prior to the 22 November *in accordance with table 3 of the document "*Reporting requirements of Individual Case Safety Reports (ICSRs) applicable to marketing authorisation holders during the interim period" (EMA/411742/2015 Rev. 9).
- **MAHs need to use EVWEB functionalities to obtain access** (and to download) **reports of suspected adverse reactions which are reported by NCAs to EVPM**. ICSRs can be downloaded as of 23 November 2017.
- **NCAs in the EEA need to submit electronically** reports of **serious suspected adverse reactions** (as referred to in paragraph 1 of Article 107a of Directive 2001/83/EC) electronically within 15 days following the receipt to EVPM.

  NCAs should stop sending ICSRs to MAHs as of 22 November 2017 (see chapter 3.1 option 3) or earlier as specified in options 1 and 2 described in chapter 3.1.
- **NCAs in the EEA need to submit electronically** within 90 days from the receipt of reports of **non-serious suspected adverse reactions** (as referred to in paragraph 1 of Article 107a of Directive 2001/83/EC) electronically to EVPM.

  NCAs should stop sending ICSRs to MAHs as of 22 November 2017 (see chapter 3.1 option 3) or earlier as specified in options 1 and 2 described in chapter 3.1.
- **EMA needs to make available promptly all suspected adverse reaction reports occurring in the EEA to the World Health Organisation.**
  NCAs should stop sending ICSRs to the WHO UMC as of 22 November 2017 (see chapter 3.1 option 3) or earlier as specified in options 1 and 2 described in chapter 3.1.

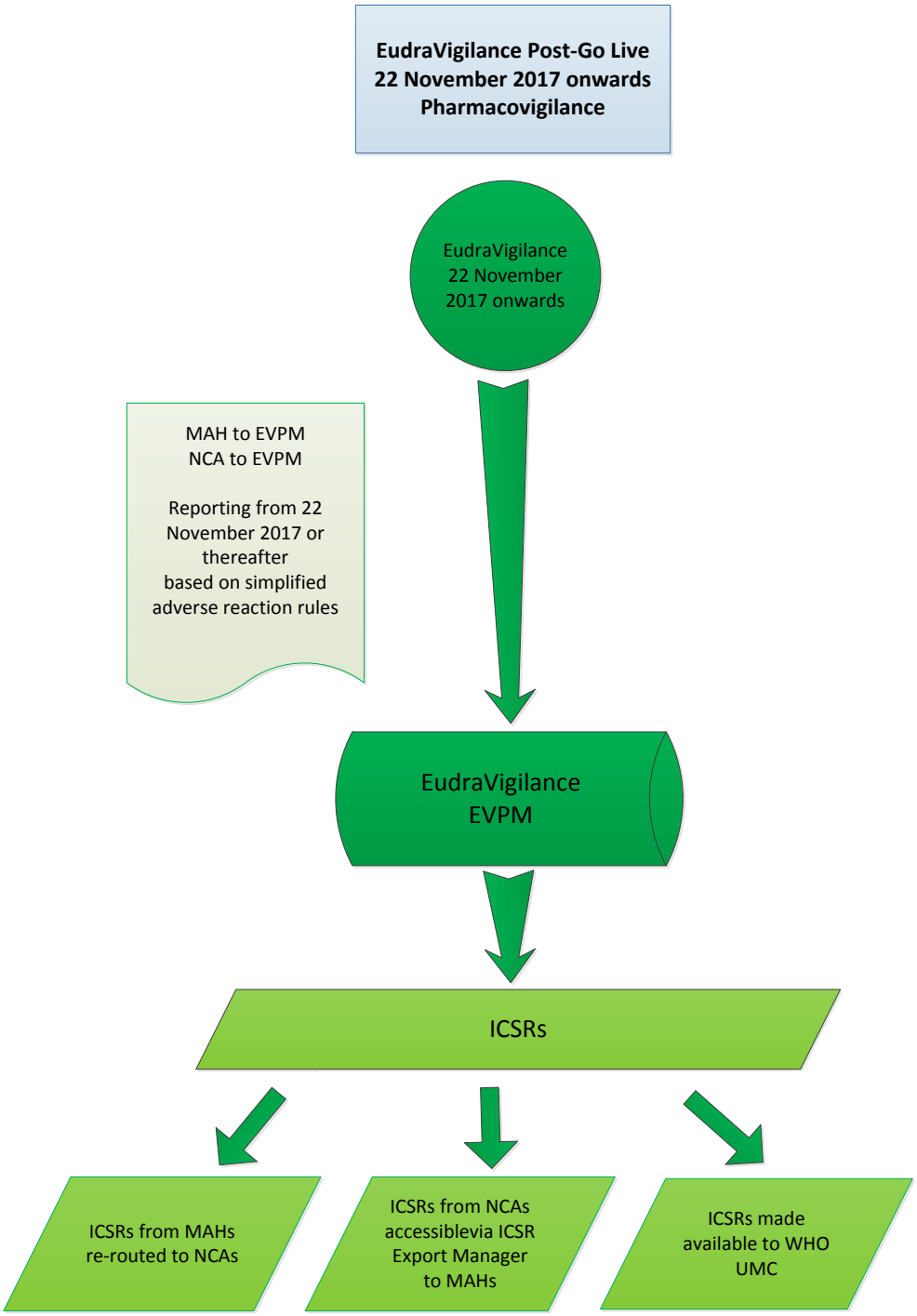


Figure 9: Electronic ADR reporting EudraVigilance post-go-live

7.3. *SUSAR reporting – clinical trials (current reporting rules)*

There will be no changes to the reporting of SUSARs during clinical trials until the application of the Clinical Trial Regulation.

Sponsors of clinical trials should **follow the current SUSAR reporting principles** set out in the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3') (2011/C 172/01) (figure 10).

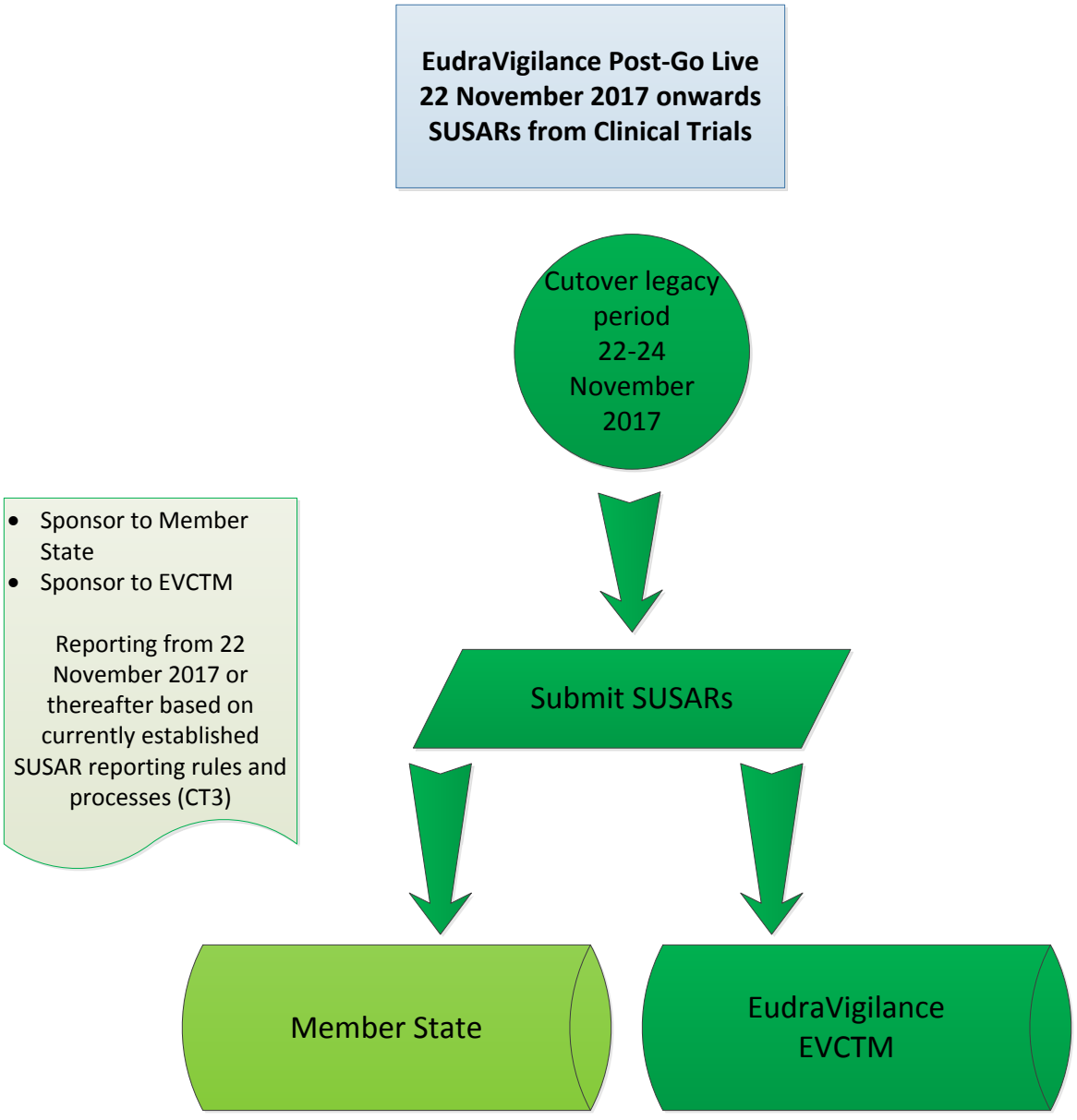


Figure 10: SUSAR reporting EudraVigilance post-go-live

7.4. *Medical literature monitoring (MLM) by the Agency*

EMA will continue the MLM service in accordance with Article 27 of Regulation (EC) No 726/2004:

- The MLM *tracking sheets* with the reference to the search and screening results *will be published* at the restricted area of the new EudraVigilance system. The same applies to the tracking sheets for valid ICSRs.
- Valid cases related to the MLM search and screening results will be entered into EVPM and made available to MAHs my means of the EVWEB ICSR download manager.

7.5. *Data submission on medicines to the XEVMPD*

MAH should submit data on medicines (Article 57) using the XEVMPD and keep this information up-to-date in accordance with Article 57 of Regulation (EC) No 726/2004.

To access the XEVMPD they should use the URL for EudraVigilance version 7.0 as follows: https://eudravigilance.ema.europa.eu/X/x.asp?XI=XH.

7.6. *Use of EVDAS/eRMRs by NCAs, EMA and MAHs*

- EMA, NCAs in the EEA should perform signal management in accordance with (GVP) Module IX – Signal management (revision 1).
- MAHs need to comply with the provisions set out in GVP) Module IX – Signal management (revision 1) and follow the alternative arrangements for a pragmatic implementation.
- EVDAS will be up to date on 25 November 2017 having processed all the ICSRs resulting from the cutover period, which should be submitted from 22 to 24 November 2017.
- Routine eRMR (6 months) for NCAs will be produced on the 22 November 2017 (reference period: 8 May to 5 November) with the hyperlinks updated for the new EudraVigilance system.
- Additional eRMR for NCAs will be produced on 29 November (the reference period will include the additional eRMR not produced on the 15 November, 23 October to 26 November 2017).
- Routine eRMRs (monthly) for NCAs will be produced on 6 December 2017 (reference period: 6 November to 3 December 2017) as initially scheduled.
- Routine eRMRs (3 months) for NCAs will be produced on 6 December 2017 (reference period: 4 September to 3 December 2017) as initially scheduled.
- Fixed eRMR (6 months) for MAHs will be produced on 22 November 2017 (reference period 1 May to 31 October 2017)
- Ad-hoc eRMR for MAHs will be produced on 24 November based on the reference period selected by the users. EVDAS will contain data up to the 7 November 2017; new ICSRs will be subsequently processed as received as of 22 November 2017.

7.7. *EudraVigilance registration application and registration of organisation/users*

The registration process of new organisations and users continues in accordance with the process described at the EudraVigilance: how to register webpage.

7.8. *Interoperability testing with the new EudraVigilance XCOMP (test) environment*

Interoperability testing with the new EudraVigilance (XCOMP) environment can continue with main focus on the ICH E2B(R3) file testing.

Organisations should refer to the following documents for the preparatory testing:

- EudraVigilance technical support plan for national competent authorities in the EEA
- EudraVigilance checklist for national competent authorities in the EEA
- EudraVigilance testing instructions and checklist for marketing authorisation holders and sponsors of clinical trials in the EEA

Organisations preparing for electronic transmissions of ICSRs to EudraVigilance for the first time or performing major upgrades to established systems should consult EudraVigilance: electronic reporting and follow the steps described. Annex: List of WEBTRADER organisations.